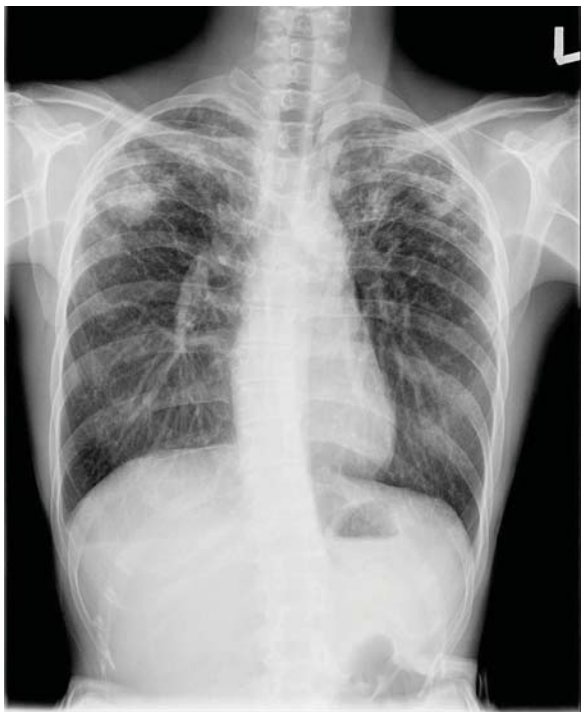
結核病處方的調整與分子抗藥檢測的時機

中華民國防癆協會理事長
台灣結核暨肺部疾病醫學會理事
萬芳醫院余明治醫師

大綱

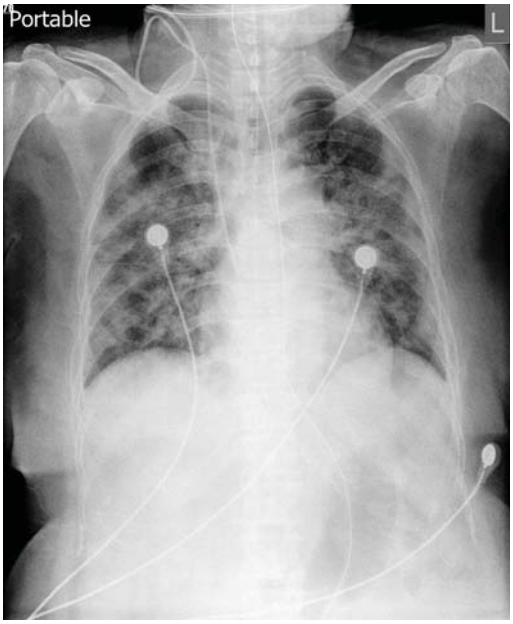
- 新冠疫情下的結核病
- 結核病的診斷與治療
- 調整處方的臨床情境
- 分子抗藥檢測的時機
- 分子檢測的其他考量
- 結論



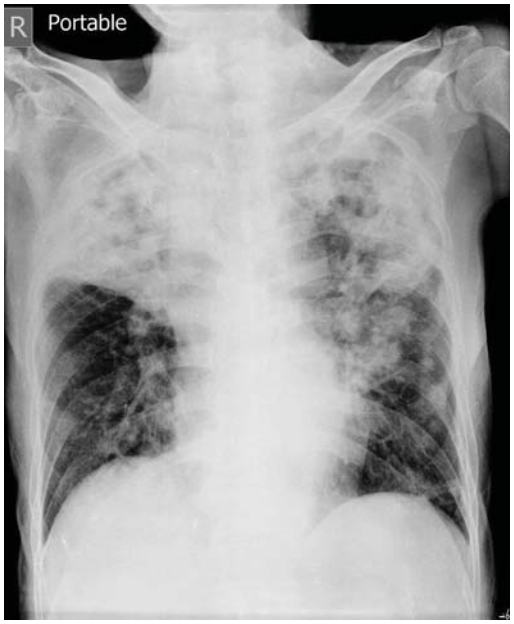
新冠疫情下的結核病

新冠疫情期間確保結核病服務

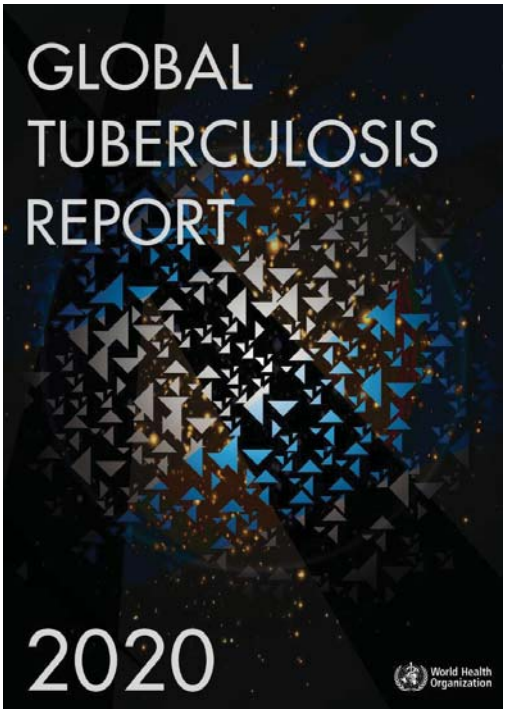
COVID-19



Far-advanced TB

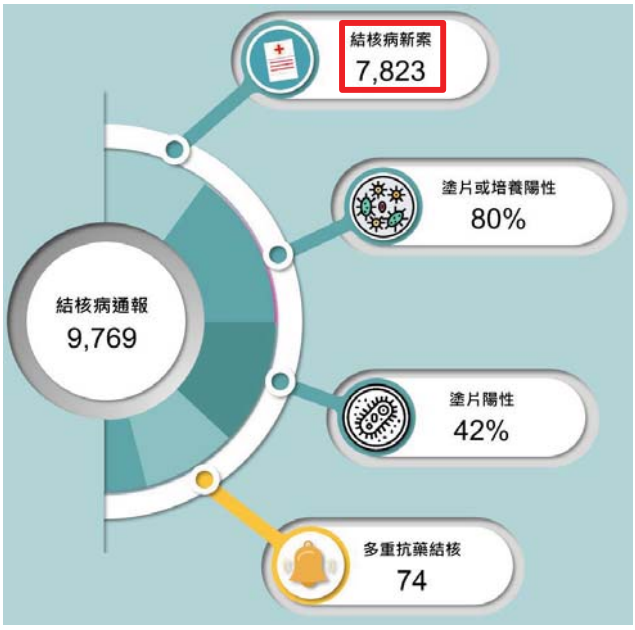


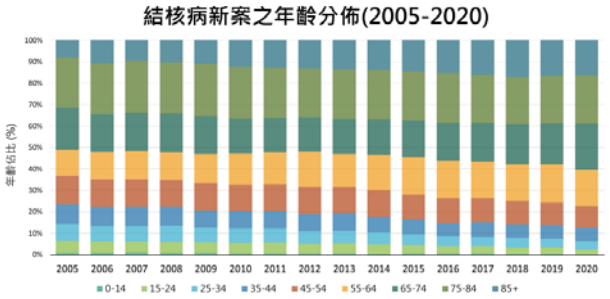
全球結核病流行概況



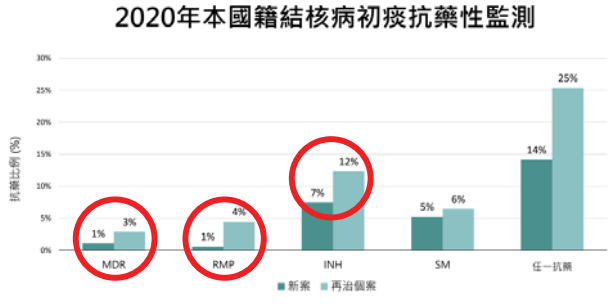
- **Globally, 2019**
  - 10.0 million TB patients
  - 1.45 million TB deaths
- **Drug-resistant TB**
  - 0.5 million rifampicin-resistant TB (RR-TB)
    - 78% multidrug-resistant TB (MDR-TB)
    - 3.3% of new TB cases
    - 17.7% of previously treated cases

台灣結核病流行概況





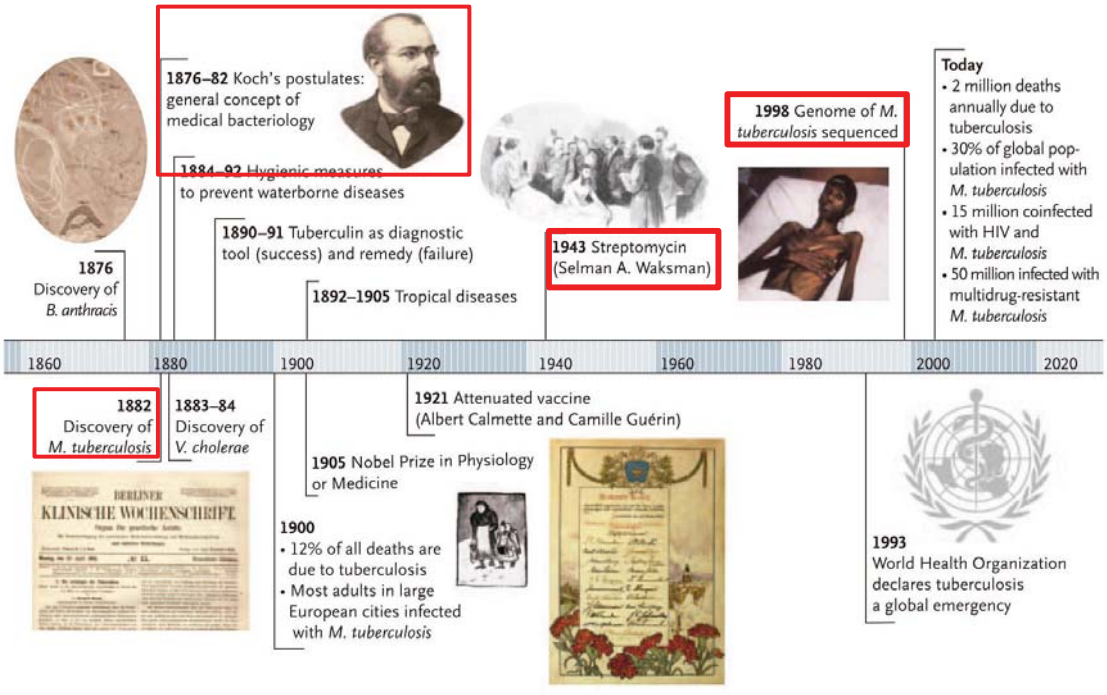
65歲以上個案占所有個案大於60%



備註：本國人抗藥比例，INH、RMP、SM抗藥，不含MDR抗藥者。

結核病的診斷與治療

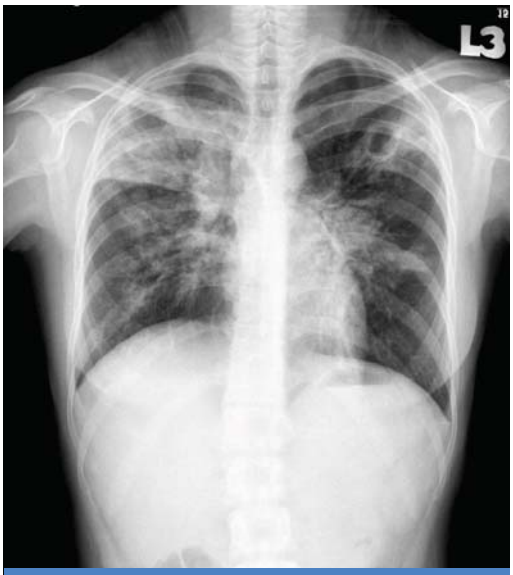
結核病歷史的重要里程碑



N Engl J Med 2005;353:2423-6

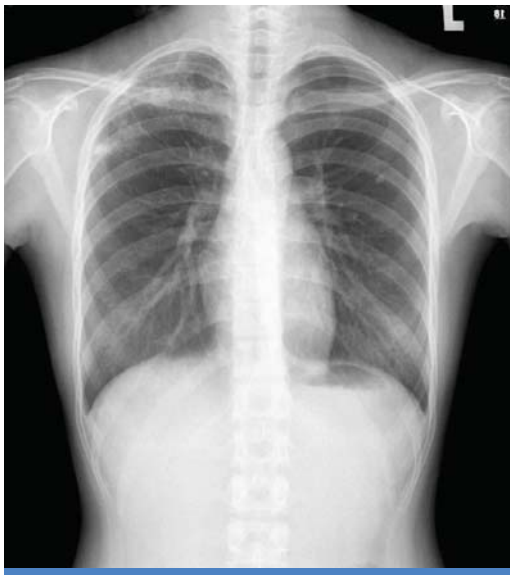
結核菌耐酸性染色與培養

Acid-fast Stain(+)/Culture(+)



5,000 to 10,000 bacilli per milliliter

Acid-fast Stain(-)/Culture(+)



10 to 100 Organisms per milliliter

核酸增幅檢驗-1996

950 MMWR November 1, 1996

Notices to Readers

Nucleic Acid Amplification Tests for Tuberculosis

Traditional methods for laboratory diagnosis of tuberculosis (TB) may require weeks, and delay can impede treatment and control efforts. Nucleic acid amplification (NAA) tests, such as polymerase chain reaction (PCR) and other methods for amplifying DNA and RNA, may facilitate rapid detection of microorganisms. An NAA test for *Mycobacterium tuberculosis* complex (Amplified Mycobacterium Tuberculosis Direct Test or MTD [Gen-Probe®, San Diego, California])* was recently approved by the Food and Drug Administration (FDA) for use on processed clinical specimens (1), and others are under development. Although NAA tests have been offered by individual laboratories, approval of commercial kits may result in increased use for clinical practice and TB control. This report summarizes potential uses of NAA tests for TB diagnosis and provides interim guidelines for the use of such tests.

Current NAA Tests and FDA-Approved Uses

The MTD test uses transcription-mediated amplification to detect *M. tuberculosis*-complex ribosomal RNA (2). The test is approved for use in conjunction with culture for respiratory specimens that are positive for acid-fast bacilli (AFB) on microscopy and were obtained from untreated patients. Based on the product label (package insert), test sensitivity in clinical trials was 95.5%, and specificity was 100%. The specificity does not indicate the growth of *M. tuberculosis* from all MTD-positive specimens; trials included MTD-positive, culture-negative specimens from patients with other positive cultures, and there are other reports of test readings "in the low range of positivity" with nontuberculous mycobacteria (2). Users should consult the label for additional information.

When used as approved, a positive MTD test result can provide relatively rapid feedback, indicating a high likelihood of TB. Some public health professionals have considered a negative result to be contributory information for prioritizing contact investigations. False-negative results may be obtained for specimens containing low numbers of *M. tuberculosis* or substances inhibiting the assay. Regardless of MTD results, mycobacterial culture is required for drug-susceptibility testing and precise species and strain identification. As approved for use on AFB-smear-positive respiratory specimens, MTD tests usually will not change the eligibility of a case for surveillance reporting; patients for whom results are positive generally would meet the surveillance case definition previously published by CDC (3).

Several other NAA tests are under commercial development, including the Roche Amplicor™ test (4), a PCR-based test that amplifies mycobacterial DNA. This test was publicly considered in January 1996 by an FDA advisory panel, which recommended approval for use similar to the MTD. If such tests are approved, principles guiding their use would be similar to those for the MTD test.

Because specimen type and clinical setting affect interpretation of NAA tests, clinicians should provide information about patients and specimens to the laboratory, and laboratory directors should provide information about local test performance and interpretation both when tests are ordered and when results are reported. Clinicians should be educated about use under local conditions (predictive values vary with

*Use of trade names and commercial sources is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

- An NAA (nucleic acid amplification) test for *Mycobacterium tuberculosis* complex
  - Approved for use in conjunction with culture for Respiratory specimens
    - Positive for acid-fast bacilli and from untreated patients
- Decisions about when and how to use NAA tests for TB diagnosis should be individualized

核酸增幅檢驗-2015

防疫學苑系列 002

結核病診治指引

Taiwan Guidelines for TB Diagnosis & Treatment

第 5.1 版

衛生福利部疾病管制署 編

主 編 陸坤泰

編輯委員群

（依姓氏筆畫排序）

王振源 王貴鳳 江振源

余明治 李仁智 李秉穎

李品慧 林錫勳 姜義新

洪健清 宋 任 詹珮君

蘇維鈞

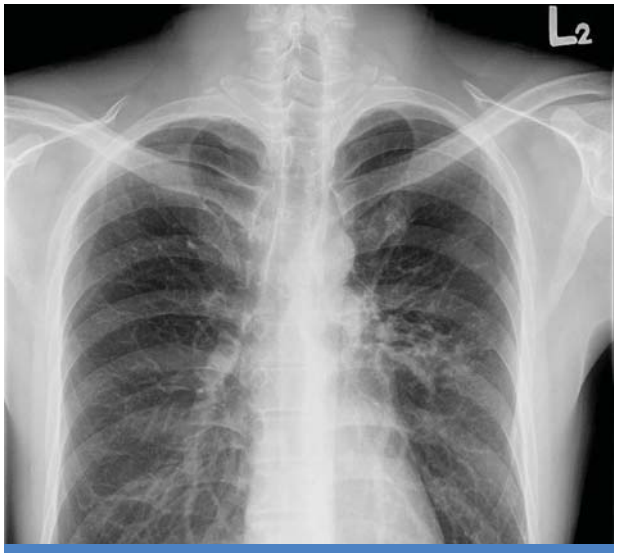
共同著作

臺灣家庭醫學醫學會 臺灣兒科醫學會 臺灣感染症醫學會

臺灣胸腔暨重症加護醫學會 臺灣內科醫學會 臺灣結核病醫學會

衛生福利部疾病管制署 出版

2015 年 1 月



AFS(-), NAA(+), Culture(+): 19 days

對於任一位臨床高度懷疑肺結核但尚未被確認或檢驗結果可能會改變處置的疑似病人，進行NAA 檢驗應是標準步驟

治療-1

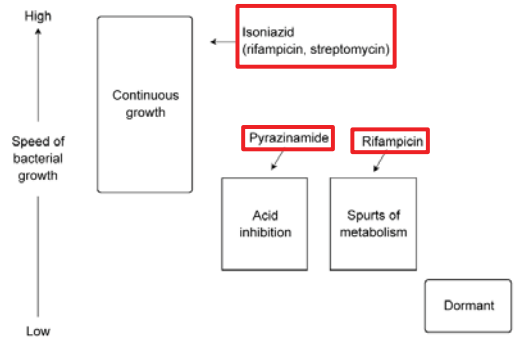


Table 8.1 Number of bacilli required for the appearance of a mutant resistant to different drugs

Isoniazid	1×10^5–10^6 bacilli
Rifampicin	1×10^7–10^8 bacilli
Streptomycin	1×10^5–10^6 bacilli
Ethambutol	1×10^5–10^6 bacilli
Pyrazinamide	1×10^2–10^4 bacilli
Fluoroquinolone	1×10^5–10^6 bacilli
Other drugs	1×10^3–10^6 bacilli

Table 8.2 Estimated bacterial populations in the different tuberculosis lesions

Smear-positive tuberculosis	10^7–10^9 bacilli
Cavitary tuberculosis	10^7–10^9 bacilli
Infiltrating	10^4–10^7 bacilli
Nodules	10^4–10^6 bacilli
Adenopathies	10^4–10^6 bacilli
Renal tuberculosis	10^7–10^9 bacilli
Extra-pulmonary tuberculosis	10^4–10^6 bacilli

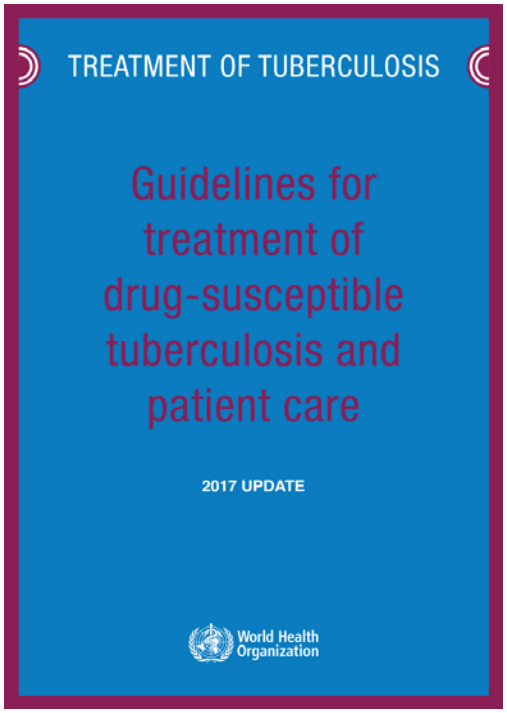
Guidelines for Clinical and Operational Management of Drug-Resistant Tuberculosis, IUATLD, 2013

Three Basic Principles

- Regimens for treatment of disease must contain multiple drugs to which the organisms are susceptible
- The drugs must be taken regularly
- Drug therapy must continue for a sufficient period of time

Am J Respir Crit Care Med 1994;149:1359-74

治療-2

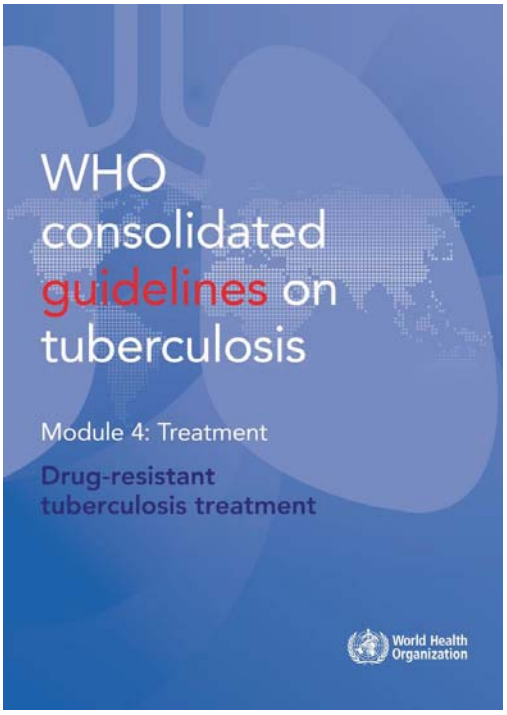


Summary of changes in the new guidelines 2017 and policy recommendations on treatment of drug-susceptible TB and patient care in other existing WHO guidelines that remain valid

Guidelines for treatment of tuberculosis, 2010[12] *(1)*	Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update
Duration of rifampicin in new TB patients	
New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR (Strong recommendation, high grade of evidence)	Remains valid*
The 2HRZE/6HE treatment regimen should be phased out (Strong recommendation, high grade of evidence)	Remains valid*
Effectiveness of shortened fluoroquinolone-containing regimens	
NO EXISTING SPECIFIC RECOMMENDATION	UPDATED* In patients with drug-susceptible pulmonary TB, 4-month fluoroquinolone-containing regimens[13] should not be used and the 6-month rifampicin-based regimen 2HRZE/4HR remains the recommended regimen (Strong recommendation, moderate certainty in the evidence)

2HERZ/4HR(E)

抗藥性結核的治療



- **Regimen for rifampicin-susceptible, isoniazid-resistant tuberculosis**
- **Shorter all-oral bedaquiline-containing regimen for multidrug- or rifampicin-resistant tuberculosis**
- **Longer regimens for multidrug- or rifampicin-resistant tuberculosis**
- **The bedaquiline, pretomanid and linezolid regimen for multidrug-resistant tuberculosis with additional fluoroquinolone resistance**
- Monitoring patient response to MDR-TB treatment using culture
- Starting antiretroviral therapy in patients on second-line antituberculosis regimens
- Surgery for patients on MDR-TB treatment
- Care and support for patients with MDR/RR-TB

藥物敏感性試驗

Essential Laboratory Tests for the Detection of Mycobacterium tuberculosis

Test	Time Required
I. Nucleic acid amplification test, detection (NAAT-TB)	1 d
II. Nucleic acid amplification test, resistance markers (NAAT-R)	1–2 d
III. Acid-fast bacilli microscopy	1 d
IV. Growth detection Liquid Solid	Up to 6–8 wk (average 10–14 d) (average 3–4 wk)
V. Identification of Mycobacterium tuberculosis complex by DNA probe or HPLC	1 d[a]
VI. First-line drug susceptibility testing (liquid medium)	1 to 2 wk[a]
VII. Second-line and novel compound drug susceptibility testing	
i. Liquid (broth-based) medium	1 to 2 wk[a]
ii. Solid (agar- or egg-based) medium	3 to 4 wk[a]

Abbreviation: HPLC, high-performance liquid chromatography.[a]After detection of growth.

Clin Infect Dis 2017;64:e1–e33

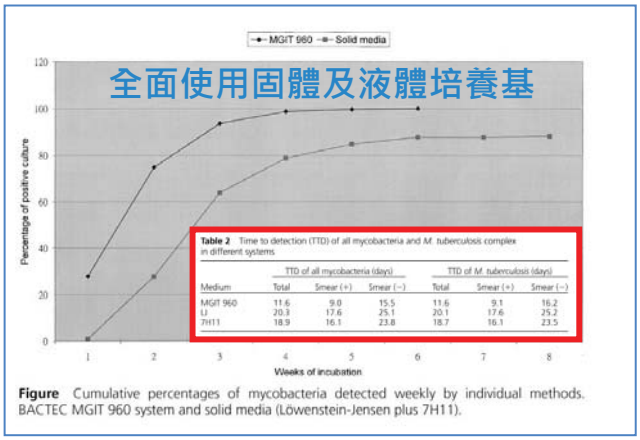
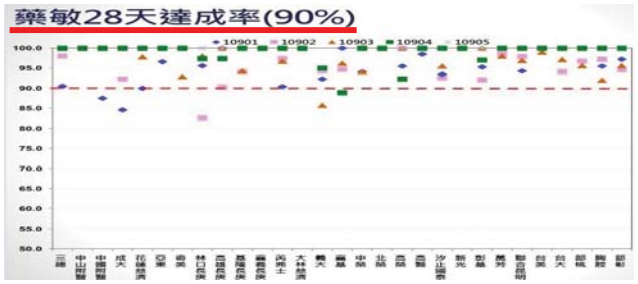
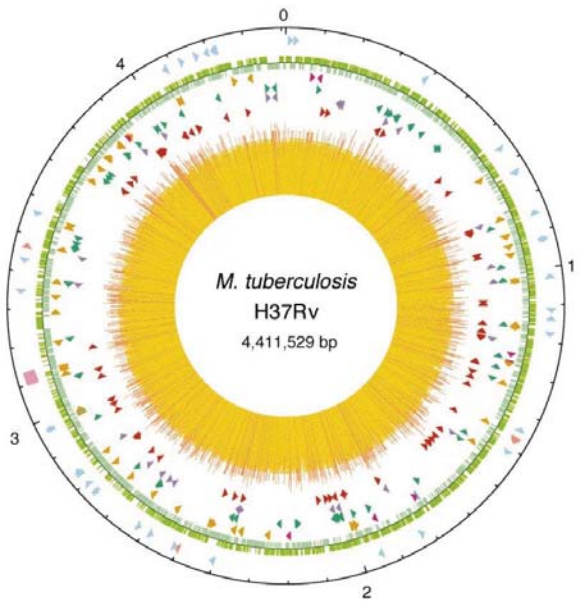


Figure Cumulative percentages of mycobacteria detected weekly by individual methods. BACTEC MGIT 960 system and solid media (Löwenstein-Jensen plus 7H11).

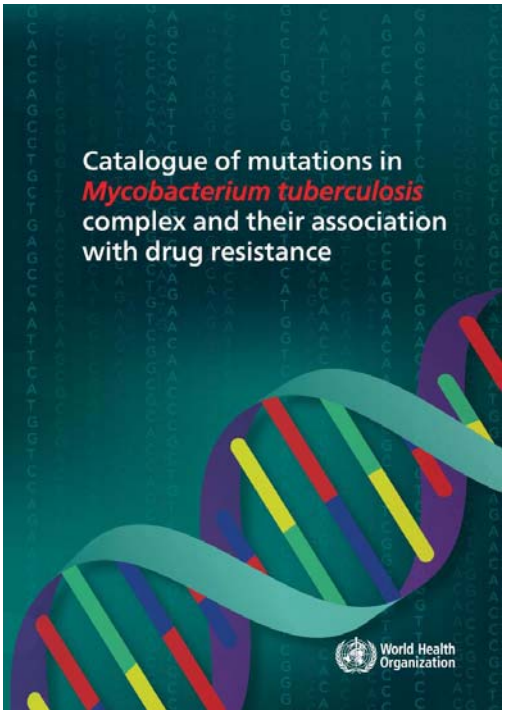
Int J Tuberc Lung Dis 2003;7:569-74



抗結核藥物的抗藥相關基因



Nature 1998;393:537–44



分子抗藥檢測

GenoType MTBDRplus Assay

2008

- Technology: PCR and the Strip technology
- Targets: rifampicin (*rpoB* gene) and isoniazid (*katG* gene: high level isoniazid resistance; *inhA* gene: low level resistance)
- Complex to perform and require technical expertise
- **Decentralizing: not applicable**

Xpert MTB/RIF Assay

2010

- Technology: Nested real-time PCR
- Targets: *rpoB* gene - probed with five molecular beacons for mutations within the rifampin-resistance determining region (RRDR)
- Two-hour detection of MTB and rifampin resistance mutations

Rifampin的快速分子檢測

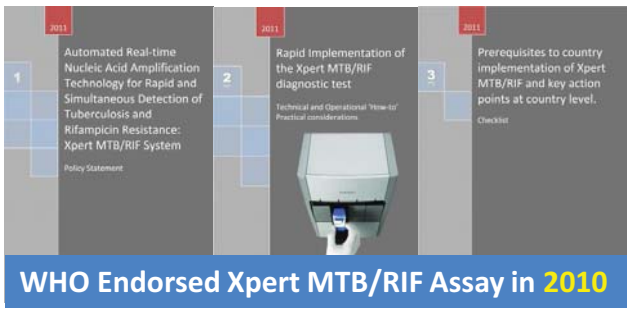
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 9, 2010 VOL. 363 NO. 11

Rapid Molecular Detection of Tuberculosis and Rifampin Resistance

Catharina C. Boehme, M.D., Pamela Nabeta, M.D., Doris Hillemann, Ph.D., Mark P. Nicol, Ph.D., Shubhada Shenai, Ph.D., Fiorella Krapp, M.D., Jenny Allen, B.Tech., Rasim Tahirli, M.D., Robert Blakemore, B.S., Roxana Rustomjee, M.D., Ph.D., Ana Milovic, M.S., Martin Jones, Ph.D., Sean M. O'Brien, Ph.D., David H. Persing, M.D., Ph.D., Sabine Ruesch-Gerdes, M.D., Eduardo Gotuzzo, M.D., Camilla Rodrigues, M.D., David Alland, M.D., and Mark D. Perkins, M.D.

ABSTRACT



WHO Endorsed Xpert MTB/RIF Assay in 2010

分子檢驗方法	2015 年認可實驗室	使用家數
羅氏達可結核桿菌測試劑 (COBAS TaqMan MTB Test)		17
賽沛結核分枝桿菌檢測試劑組 GeneXpert MTB/RIF test		11
"飛迅"結核桿菌快速檢驗試劑（未滅菌） FastSure TB Rapid Test		2
晶宇結核分枝桿菌群檢驗試劑套組及生物晶片檢測平臺 DR. MTBC ScreenTM IVD Kit and DR. AimTM Platform		9
亞洲基因結核分枝桿菌核酸探針檢驗試劑 AsiaGen Mycobacterium tuberculosis Detection Kit		2
"必帝"結核桿菌測試劑（未滅菌） "BD"ProbeTec ET Mycobacterium tuberculosis reagents (Non-Sterile)		1
In-house PCR		2

疫情報導 2017 年 第 33 卷·第 20 期

台灣結核病診治指引

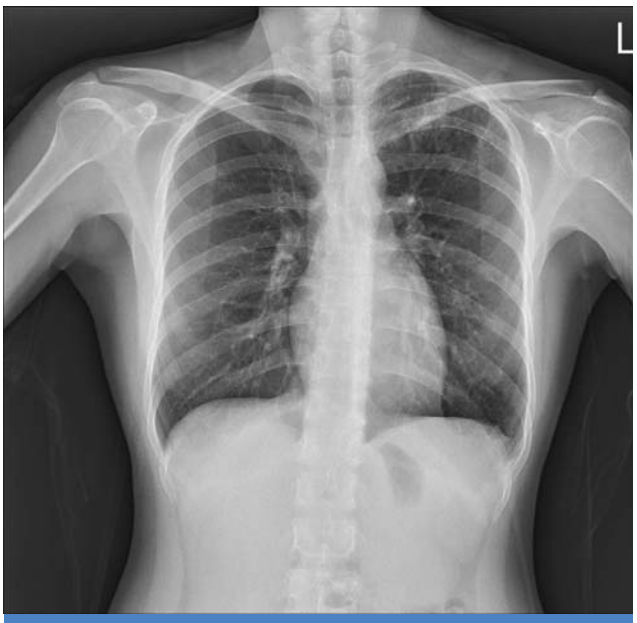
第一線抗結核藥物感受性試驗	• 第一次培養陽性的結核菌株 • 治療第五個月及以後培養陽性 • 陰轉後再度培養陽性
快速分子檢測	• 抗藥性的高危險族群

The proportion of patients with DST results in the national TB registry was 97.9% (97.9% among new and 100.0% among recurrent cases) in 2016

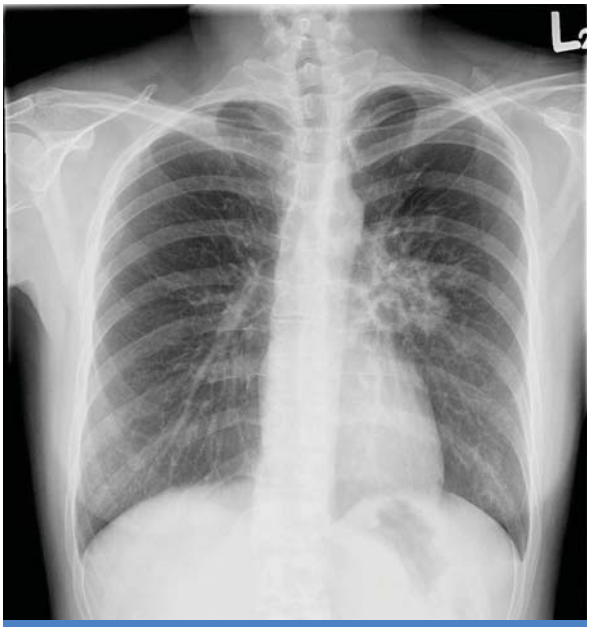
PLoS ONE 2019;14(4): e0214792

調整處方的臨床情境

開始治療：2HERZ/4HR(E)

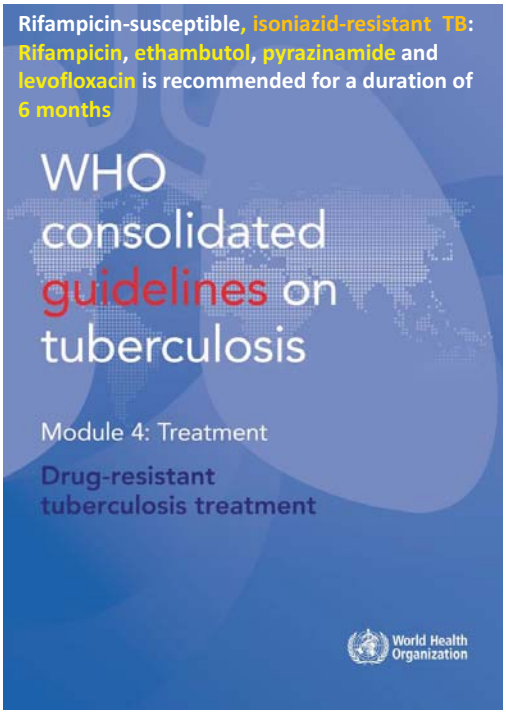


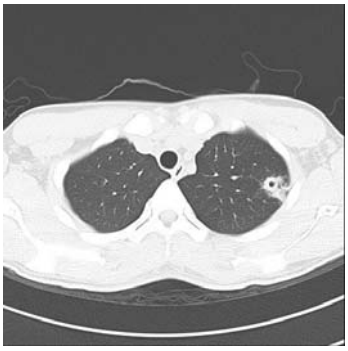
Acid-fast stain (-)

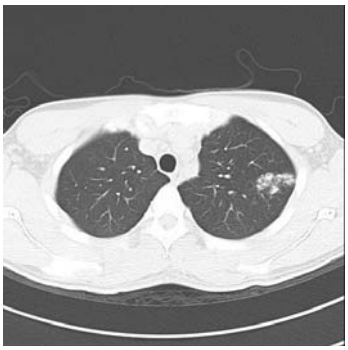


Acid-fast stain (++++)

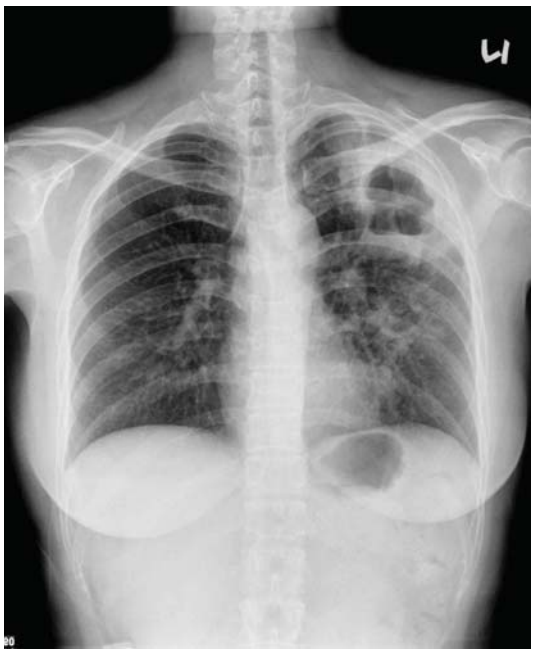
抗藥性：H/E抗藥接觸者







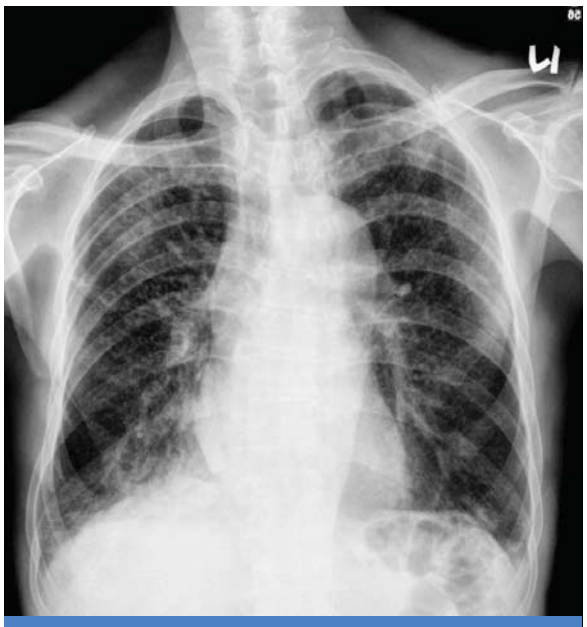
共病： DM + Hepatitis B



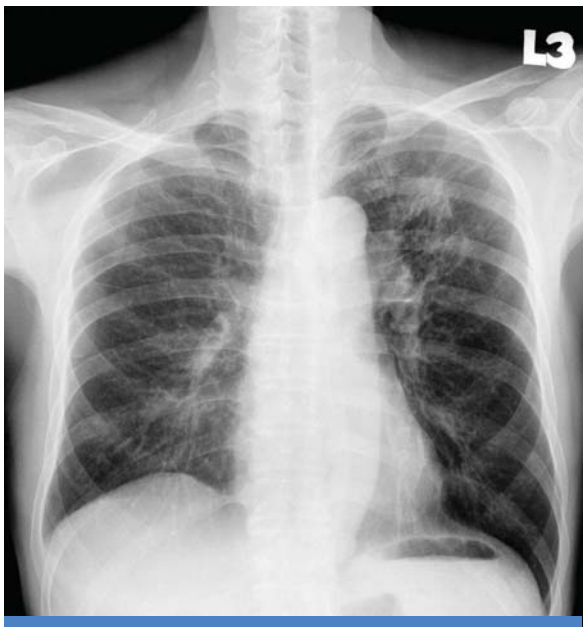
- HBsAg (+), Anti-HCV (-)
- AST: 310 U/L
- ALT: 451 U/L
- Sugar: 396 mg/dL

- 抗結核藥物
  - HERZ ?

治療中調整處方：副作用/抗藥性



治療8星期：精神可/食慾好
AST: 296 U/L, ALT: 282U/L



Pulmonary TB: Isolation
MDR-TB: Isolation again

Adding Moxifloxacin is Associated with a Shorter Time to Culture Conversion in Pulmonary Tuberculosis

Table 2 Baseline laboratory results, radiographic features and treatment modification

Characteristic	MXF group (n = 51) n (%)	HERZ group (n = 72) n (%)	OR (95%CI)	P value*
Sputum acid-fast smear-positive	41 (80)	57 (79)	1.1 (0.4–2.6)	0.87
M. tuberculosis isolate resistant to any first-line drug	8 (16)	7 (10)	1.7 (0.6–5.1)	0.32
Resistant to H and E	0	1		
Resistant to H	7	5		
Resistant to E	1	1		
Haemoglobin <11 g/dl	16 (31)	31 (43)	0.6 (0.3–1.3)	0.19
Albumin <3.5 g/dl	13 (26)	29 (40)	0.5 (0.2–1.1)	0.09
Total bilirubin ⩾1.5 mg/dl	8 (16)	6 (8)	2.1 (0.7–6.3)	0.21
Alanine aminotransferase >40 U/l	6 (12)	14 (19)	0.6 (0.2–1.6)	0.26
Creatinine ⩾1.5 mg/dl	5 (10)	13 (18)	0.5 (0.2–1.5)	0.20
Bilateral lung involvement	25 (49)	41 (57)	0.7 (0.4–1.5)	0.39
Cavitation on chest film	25 (49)	25 (35)	1.8 (0.9–3.8)	0.11
Miliary lesion on chest film	7 (14)	7 (10)	1.5 (0.5–4.5)	0.49
Anti-tuberculosis regimen modified	22 (43)	29 (40)	1.1 (0.5–2.3)	0.75
Modified before culture conversion	6 (12)	12 (17)	0.7 (0.2–1.9)	0.45

Int J Tuberc Lung Dis 2010;14:65–71

INT J TUBERC LUNG DIS 17(11):1435–1441

http://dx.doi.org/10.5588/ijtld.13.0182

Monitoring changes in anti-tuberculosis treatment: associated factors determined at the time of diagnosis

M. N. Altet,*†‡ R. Vidal,†§ C. Milá,*†§ T. Rodrigo,†¶# M. Casals,‡¶ I. Mir,†¶ J. Ruiz-Manzano,†,**,†† M. A. Jiménez-Fuentes,*†§ F. Sánchez,†,‡‡ J. Maldonado,†,§§ R. Blanquer,†,¶¶ M. L. de Souza-Galvão,*†‡§ J. Solsona,*†§ E. Azlor,‡ D. Díaz,†,## J. L. Calpe,†,*** J. A. Caylá†,#,†††

*Unidad de Prevención y Control de la Tuberculosis de Barcelona, Barcelona, †Programa Integrado de Investigación en Tuberculosis de la Sociedad Española de Neumología y Cirugía Torácica, Barcelona, ‡Institut de Recerca en Atenció Primària, Barcelona, §Hospital Universitario Vall d'Hebrón, Barcelona, ¶Hospital Universitari Son Llàtzer, Mallorca, #Centro de Investigación Biomédica en Red (CIBER) de Epidemiologia y Salut Pública, Madrid, **Hospital Universitari Germans Trias i Pujol de Badalona, Badalona, ††CIBER de Enfermedades Respiratorias, Mallorca, ‡‡Hospital del Mar, Barcelona, §§Unidad de Tratamiento Directamente Observado Serveis Clinics, Barcelona, ¶¶Hospital Universitari Dr Peset de Valencia, Valencia, ##Complejo Hospitalario Juan Canalejo, La Coruña, ***Hospital Marina Baixa de Alicante, Alicante, †††Unidad de Investigación en Tuberculosis de Barcelona, Servicio de Epidemiología de la Agencia de Salud Pública de Barcelona, Barcelona, Spain

SUMMARY

OBJECTIVES: To determine predictive factors for changes in standard anti-tuberculosis chemotherapy at the time of diagnosis.

METHODS: A prospective study was performed among tuberculosis (TB) patients treated at specialised centres during 2008–2009. Treatment outcome was monitored per standard guidelines. Treatment was considered successful if the patient was cured or completed treatment. Factors associated with treatment modification were analysed at the bivariate and multivariate levels using logistic regression.

RESULTS: A total of 427 patients were included in the study. The initial standard treatment regimen was retained for 249 patients (58.3%), extended to 9 months for 36 (8.4%) and changed for 142 (33.3%). Factors associated with a change of regimen at the multivariate level were female sex, age ⩾50 years, human immunodeficiency virus infection, comorbidities, alcoholism, hospitalisation and culture-positive sputum. Drug resistance and toxicity were analysed independently. Treatment outcome was successful in 97.2% of cases without a regimen change and in 87.3% of those with a changed regimen ($P < 0.001$).

CONCLUSION: Factors associated with changes in the initial anti-tuberculosis regimen should be considered for rigorous follow-up. Results obtained through individualised treatment provided by specialists were good despite the complexity of the cases treated.

KEY WORDS: standard regimen; predictive factors; adverse reactions; MDR-TB; treatment outcomes

副作用處理原則

- **處理原則**
  - 發生藥物不良反應，應根據該不良反應的嚴重度處理
- **三層級**
  - 密切觀察即可，不必停藥
  - 症狀治療即可，不必停藥
  - 須停藥
    - 若非常確定該不良反應是由某一特定結核藥物所致，可以直接停止該藥；否則建議停止所有抗結核藥物
    - 不良反應消失或減緩後，逐一嘗試用藥找出導致此不良反應之藥物，此後不再使用該藥物

台灣結核病診治指引第6版，2017

不良反應之後處理調整的建議-1

無法使用的藥物	同類替代藥物	無藥敏結果	藥敏結果已知
H	---	9REZS	9REZ
R	B	2HBEZ / 4HB	2HBEZ / 4HB
	無法使用 B	2HEZS / 16HEZ*	18HEZ*
E	---	2HRZ / 4HR	2HRZ / 4HR
Z	---	9HRE	9HR(E)
HR	B	9BEZS	9BEZ
	無法使用 B	6EZQKT / 12EZQT*	18EZQT(S)*
HE	---	2RZKQT / 7RZQ	9RZQ
RE	B	2HBZ / 4HB	2HBZ / 4HB
	無法使用 B	4HZQKT / 8HZQ*	12HZQ(S)*#
EZ	---	2HRQKT / 7HRQ	9HR(S)
HZ	---	2REQKT / 7REQ	9REQ(S)
RZ	B	9HBE	9HBE
	無法使用 B	6HEQKT / 12HEQ*†	18HEQ(S)*†
HEZ	---	2RQKT / 7RQT	9RQT(S)

E: ethambutol; H: isoniazid; Q: fluoroquinolone; R: rifampin; B: rifabutin; S: streptomycin; T: prothionamide; Z: pyrazinamide;

台灣結核病診治指引第6版，2017

不良反應之後處理調整的建議-2

- 因不良反應而無法使用RMP時
  - 應嘗試以Rifabutin來取代RMP治療
- 使用FQ時
  - 務必確認處方中有足夠種類藥物，以避免產生FQ續發性抗藥
- 有藥物不良反應，又遇上治療反應不佳時
  - 務必重新審視是否另有抗藥性的問題
  - 應考慮加上兩種或三種以上替代藥物

台灣結核病診治指引第6版，2017

分子抗藥檢測的時機

Diagnosis of Tuberculosis in Adults and Children

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines

- Should rapid molecular drug susceptibility testing for isoniazid and rifampin be performed as part of the initial diagnostic evaluation for all patients suspected of having pulmonary TB or only in selected subgroups?
- Recommendations
  - (1) have been treated for tuberculosis in the past
  - (2) were born in or have lived for at least 1 year in a foreign country with at least a moderate tuberculosis incidence (≥20 per 100 000) or a high primary MDR-TB prevalence (≥2%)
  - (3) are contacts of patients with MDR-TB
  - (4) are HIV infected

Clin Infect Dis 2017;64:e1–e33

Treatment of Drug-Resistant Tuberculosis

An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline

- When rifampin resistance is detected
  - Additional DST should be performed immediately for first-line drugs, fluoroquinolones, and aminoglycosides

Am J Respir Crit Care Med 2019;200:e93–e142

Clinical Infectious Diseases

MAJOR ARTICLE

Treatment Outcomes of Multidrug-Resistant Tuberculosis in Taiwan: Tackling Loss to Follow-up

Ming-Chih Yu,[1,2,3,a] Chen-Yuan Chiang,[1,3,4,b] Jen-Jyh Lee,[3,b] Shun-Tien Chien,[4] Chou-Jui Lin,[5] Shih-Wei Lee,[5] Chih-Bin Lin,[5] Wen-Ta Yang,[8,9] Ying-Hsun Wu,[6] and Yi-Wen Huang[10,11,a]

[1]Division of Pulmonary Medicine, Department of Internal Medicine, Wan Fang Hospital, [2]School of Respiratory Therapy, College of Medicine, and [3]Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taiwan; [4]International Union Against Tuberculosis and Lung Disease, Paris, France; and [5]Department of Internal Medicine, Buddhist Tzu Chi General Hospital, Tzu Chi University, Hualien, [6]Chest Hospital, Ministry of Health and Welfare, Tainan, [7]Tao-Yuan General Hospital, Ministry of Health and Welfare, [8]Taichung Hospital, Ministry of Health and Welfare, [9]China Medical University, Taichung, [10]Chang-Hua Hospital, Ministry of Health and Welfare, and [11]Institute of Medicine, Chang Shan Medical University, Taichung, Taiwan

Background. The proportion of treatment success among patients with multidrug-resistant tuberculosis (MDR-TB) enrolled between 1992 and 1996 was 51.2%, and that among patients enrolled between 2000 and April 2007 was 61%. To address the challenge of MDR-TB, the Taiwan MDR-TB Consortium (TMTC) was established in May 2007. To assess the performance of the TMTC, we analyzed the data of patients enrolled in its first 5 years.

Methods. Comprehensive care was provided at no cost to patients, who were usually hospitalized for 1 month initially. Treatment regimens consisted of 4–5 drugs and the duration of treatment was 18–24 months. A case manager and a directly observed therapy provider were assigned to each patient. Psychosocial support was provided to address emotional stress and stigma. Financial support was offered to avoid the financial hardship faced by patients and their families. We assessed treatment outcomes at 30 months using internationally recommended outcome definitions.

Results. Of the 692 MDR-TB patients, 570 (82.4%) were successfully treated, 84 (12.1%) died, 18 (2.6%) had treatment failure, and 20 (2.9%) were lost to follow-up. Age ≥65 years (adjusted odds ratio [aOR], 6.78 [95% confidence interval {CI}, 3.14–14.63]), cancer (aOR, 11.82 [95% CI, 5.55–25.18]), and chronic kidney disease (aOR, 3.62 [95% CI, 1.70–7.71]) were significantly associated with death. Resistance to fluoroquinolone (aOR, 10.89 [95% CI, 3.97–29.88]) was significantly associated with treatment failure.

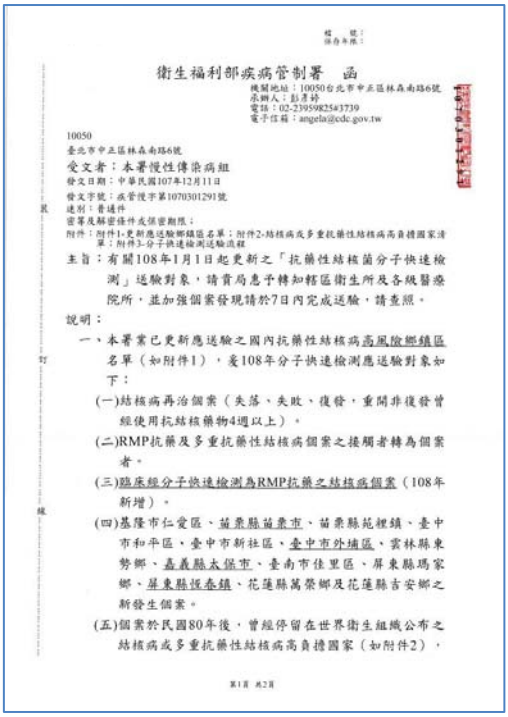
Conclusions. The TMTC, which operates under a strong collaboration between the public health authority and clinical teams, has been a highly effective model of care in the management of MDR-TB.

Keywords. tuberculosis; multidrug resistance; MDR; outcome.

Resistance to fluoroquinolone was significantly associated with treatment failure

分子快速檢測送驗對象-2020

- 1. 結核病再治個案(失落、失敗、復發，重開非復發曾經使用抗結核藥物 4 週以上)
- 2. RR-TB 及 MDR-TB 個案之接觸者轉為個案者
- 3. 臨床經分子快速檢測為RMP抗藥之結核病個案
- 4. 國內高風險地區之新發生個案
- 5. 於民國 80 年後，個案過去曾停留在疾病管制署指定應送分子快速篩檢國家，於 1 年內累積達 1 個月以上(即連續任 365 天內，停留時間累積達 30 天以上)



衛生福利部疾病管制署 函

地址：10050臺北市中正區林森南路6號
聯絡人：彭彥玲
電話：02-23959825#3739
電子信箱：angela@cdc.gov.tw

10050
臺北市中正區林森南路6號

受文者：本署慢性傳染病組
發文日期：中華民國107年12月11日
發文字號：疾管慢字第1070301291號
速別：普通件
密等及解密條件或保密期限：
附件：附件1-更新應送驗鄉鎮區名單；附件2-結核病或多重抗藥性結核病高負擔國家清單；附件3-分子快速檢測送驗流程

主旨：有關108年1月1日起更新之「抗藥性結核菌分子快速檢測」送驗對象，請貴局惠予轉知轄區衛生所及各級醫療院所，並加強個案發現請於7日內完成送驗，請查照。

說明：

一、本署業已更新應送驗之國內抗藥性結核病高風險鄉鎮區名單（如附件1），及108年分子快速檢測應送驗對象如下：

(一)結核病再治個案（失落、失敗、復發，重開非復發曾經使用抗結核藥物4週以上）。

(二)RMP抗藥及多重抗藥性結核病個案之接觸者轉為個案者。

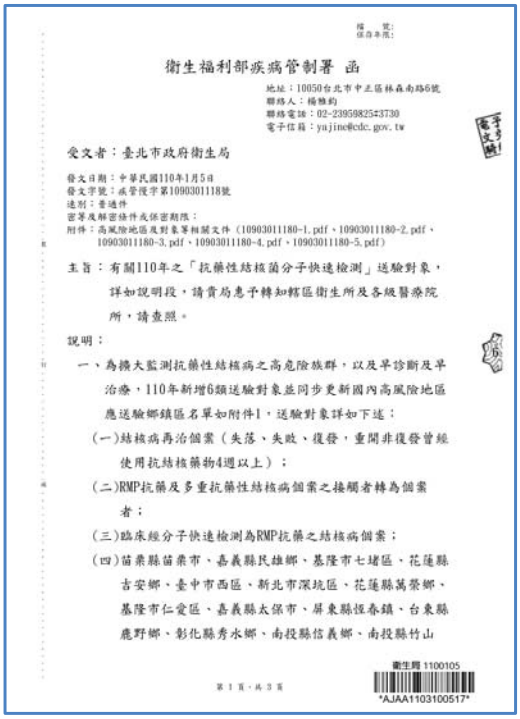
(三)臨床經分子快速檢測為RMP抗藥之結核病個案（108年新增）。

(四)基隆市仁愛區、苗栗縣苗栗市、苗栗縣苑裡鎮、臺中市和平區、臺中市新社區、臺中市外埔區、雲林縣東勢鄉、嘉義縣太保市、臺南市佳里區、屏東縣瑪家鄉、屏東縣恆春鎮、花蓮縣萬榮鄉及花蓮縣吉安鄉之新發生個案。

(五)個案於民國80年後，曾經停留在世界衛生組織公布之結核病或多重抗藥性結核病高負擔國家（如附件2），

第1頁 共2頁

分子快速檢測送驗對象-2021



衛生福利部疾病管制署 函

地址：10050台北市中正區林森南路6號
聯絡人：楊雅鈞
聯絡電話：02-23959825#3730
電子信箱：yajine@cdc.gov.tw

受文者：臺北市政府衛生局

發文日期：中華民國110年1月5日
發文字號：疾管慢字第1090301118號
速別：普通件
密等及解密條件或保密期限：
附件：高風險地區及對象等相關文件（10903011180-1.pdf、10903011180-2.pdf、10903011180-3.pdf、10903011180-4.pdf、10903011180-5.pdf）

主旨：有關110年之「抗藥性結核菌分子快速檢測」送驗對象，詳如說明段，請貴局惠予轉知轄區衛生所及各級醫療院所，請查照。

說明：

一、為擴大監測抗藥性結核病之高危險族群，以及早診斷及早治療，110年新增6類送驗對象並同步更新國內高風險地區應送驗鄉鎮區名單如附件1，送驗對象詳如下述：

(一)結核病再治個案（失落、失敗、復發，重開非復發曾經使用抗結核藥物4週以上）；

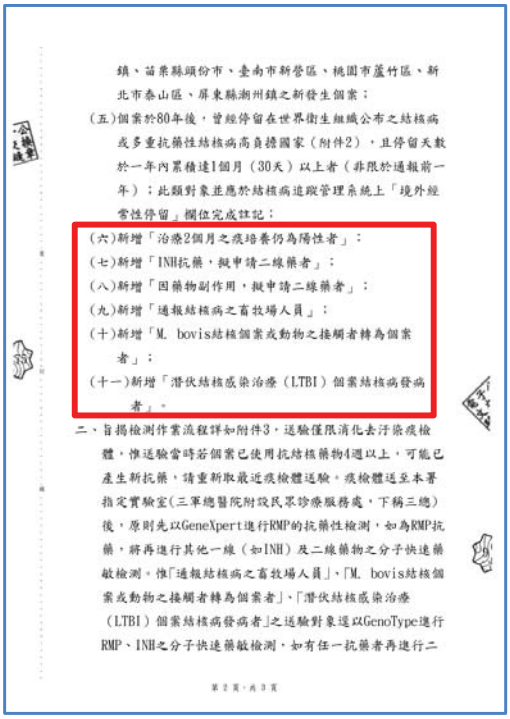
(二)RMP抗藥及多重抗藥性結核病個案之接觸者轉為個案者；

(三)臨床經分子快速檢測為RMP抗藥之結核病個案；

(四)苗栗縣苗栗市、嘉義縣民雄鄉、基隆市七堵區、花蓮縣吉安鄉、臺中市西區、新北市深坑區、花蓮縣萬榮鄉、基隆市仁愛區、嘉義縣太保市、屏東縣恆春鎮、台東縣鹿野鄉、彰化縣秀水鄉、南投縣信義鄉、南投縣竹山

衛生局 1100105
AJAA1103100517

第1頁，共3頁



鎮、苗栗縣頭份市、臺南市新營區、桃園市蘆竹區、新北市泰山區、屏東縣潮州鎮之新發生個案；

(五)個案於80年後，曾經停留在世界衛生組織公布之結核病或多重抗藥性結核病高負擔國家（附件2），且停留天數於一年內累積達1個月（30天）以上者（非限於通報前一年）；此類對象並應於結核病追蹤管理系統上「境外經常性停留」欄位完成註記；

(六)新增「治療2個月之痰培養仍為陽性者」；

(七)新增「INH抗藥，擬申請二線藥者」；

(八)新增「因藥物副作用，擬申請二線藥者」；

(九)新增「通報結核病之畜牧場人員」；

(十)新增「M. bovis結核個案或動物之接觸者轉為個案者」；

(十一)新增「潛伏結核感染治療（LTBI）個案結核病發病者」。

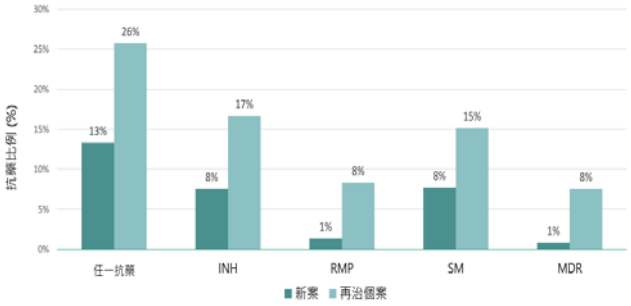
二、旨揭檢測作業流程詳如附件3，送驗僅限清化去汙染痰檢體，惟送驗當時若個案已使用抗結核藥物4週以上，可能已產生新抗藥，請重新取最近痰檢體送驗。痰檢體送至本署指定實驗室(三軍總醫院附設民眾診療服務處，下稱三總)後，原則先以GeneXpert進行RMP的抗藥性檢測，如為RMP抗藥，將再進行其他一線（如INH）及二線藥物之分子快速藥敏檢測。惟「通報結核病之畜牧場人員」、「M. bovis結核個案或動物之接觸者轉為個案者」、「潛伏結核感染治療（LTBI）個案結核病發病者」之送驗對象還以GenoType進行RMP、INH之分子快速藥敏檢測，如有任一抗藥者再進行二

第2頁，共3頁

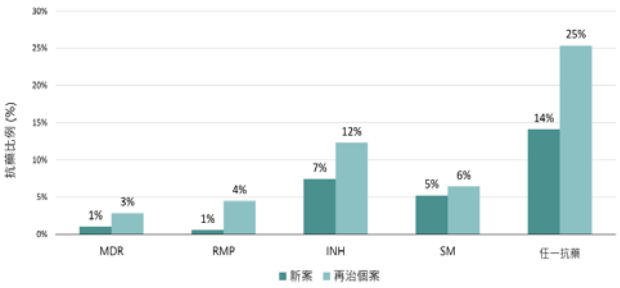
1. 結核病再治個案-1

(失落、失敗、復發，重開非復發曾經使用抗結核藥物4週以上)

2019年結核病抗藥性監測



2020年本國籍結核病初痰抗藥性監測



備註：本國人抗藥比例，INH、RMP、SM抗藥，不含MDR抗藥者。

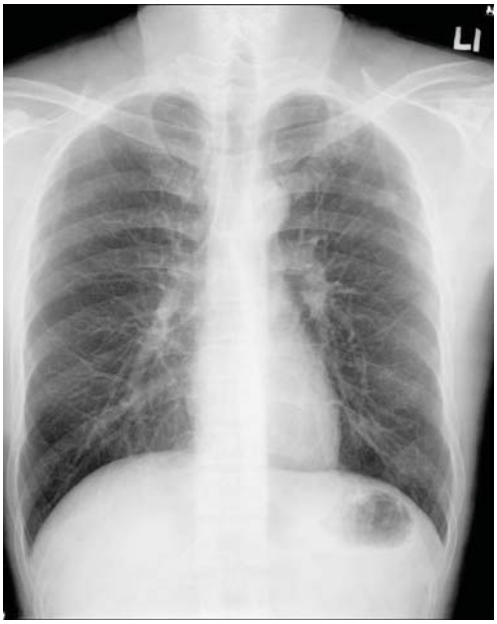
- Patients who have interrupted first-line TB treatment or have had recurrence of disease tend to have a higher risk of drug resistance than new TB patients
- Patients eligible for retreatment should be referred for a rapid molecular test or drug susceptibility testing to determine at least rifampicin resistance, and preferably also isoniazid resistance status

Guidelines for Treatment of Drug-Susceptible Tuberculosis and Patient Care, WHO, 2017 update

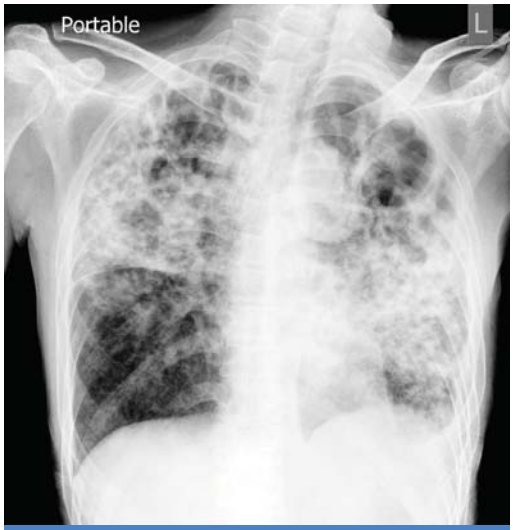
1. 結核病再治個案-2

(失落、失敗、復發，重開非復發曾經使用抗結核藥物4週以上)

2011



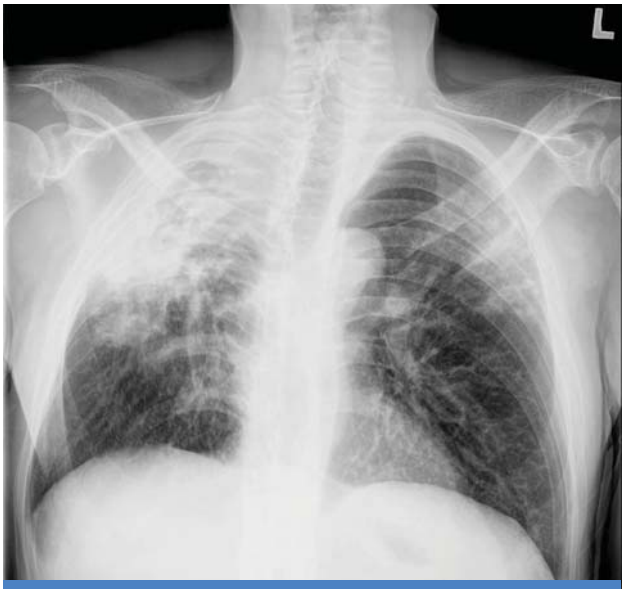
2014



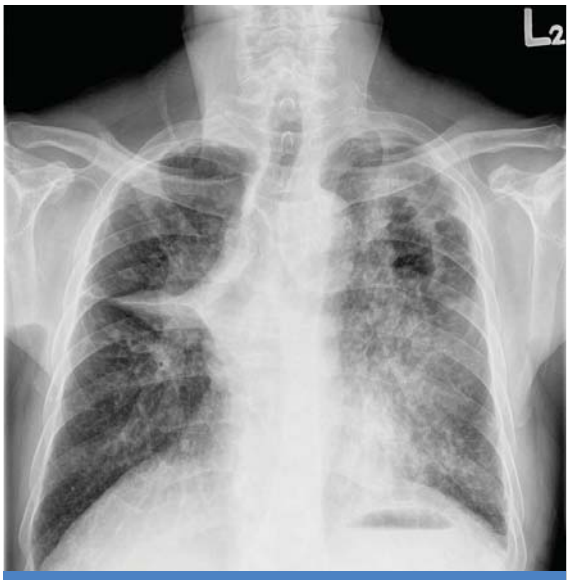
X-pert: RMP-R
DST: R-R, HES-S

1. 結核病再治個案-3

(失落、失敗、復發，重開非復發曾經使用抗結核藥物4週以上)



規則治療3個月
DST從INH-R到INH-R/RMP-R



TB History/Pneumoconiosis
Xpert: RMP-R; GenoTypeMTBDR*plus:* H-S, R-R
Phenotypic DST: HR-R

2. 曾為RMP抗藥及MDR-TB接觸者之個案-1

Tuberculosis burden in households of patients with multidrug-resistant and extensively drug-resistant tuberculosis: a retrospective cohort study

Mercedes C Becerra, Sasha C Appleton, Molly F Franke, Katiuska Chalco, Fernando Arteaga, Jaime Bayona, Megan Murray, Sidney S Atwood, Carole D Mitnick

Summary

Background Multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis have emerged as major global health threats. WHO recommends contact investigation in close contacts of patients with MDR and XDR tuberculosis. We aimed to assess the burden of tuberculosis disease in household contacts of such patients.

Methods We undertook a retrospective cohort study of household contacts of patients treated for MDR or XDR tuberculosis in Lima, Peru, in 1996–2003. The primary outcome was active tuberculosis in household contacts at the time the index patient began MDR tuberculosis treatment and during the 4-year follow-up. We examined whether the occurrence of active tuberculosis in the household contacts differed by resistance pattern of the index patient: either MDR or XDR tuberculosis.

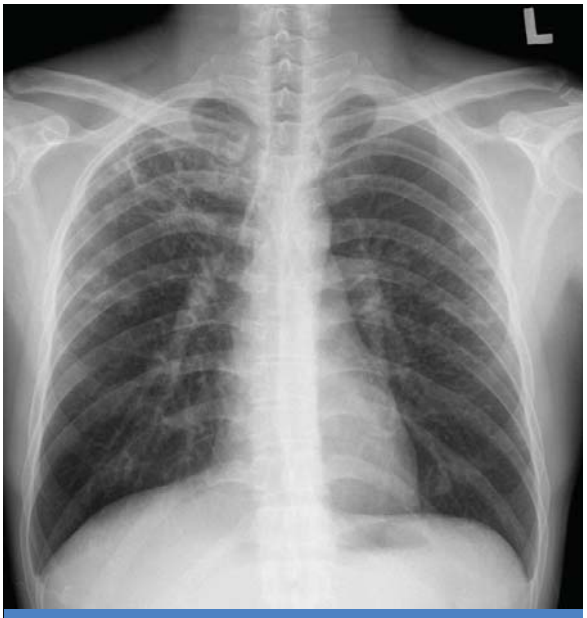
Findings 693 households of index patients with MDR tuberculosis were enrolled in the study. In 48 households, the *Mycobacterium tuberculosis* isolate from the index patient was XDR. Of the 4503 household contacts, 117 (2·60%) had active tuberculosis at the time the index patient began MDR tuberculosis treatment—there was no difference in prevalence between XDR and MDR tuberculosis households. During the 4-year follow-up, 242 contacts developed active tuberculosis—the frequency of active tuberculosis was nearly two times higher in contacts of patients with XDR tuberculosis than it was in contacts of patients with MDR tuberculosis (hazard ratio 1·88, 95% CI 1·10–3·21). In the 359 contacts with active tuberculosis, 142 (40%) had had isolates tested for resistance against first-line drugs, of whom 129 (90·9%, 95% CI 85·0–94·6) had MDR tuberculosis.

Interpretation In view of the high risk of disease recorded in household contacts of patients with MDR or XDR tuberculosis, tuberculosis programmes should implement systematic household contact investigations for all patients identified as having MDR or XDR tuberculosis. If shown to have active tuberculosis, these household contacts should be suspected as having MDR tuberculosis until proven otherwise.

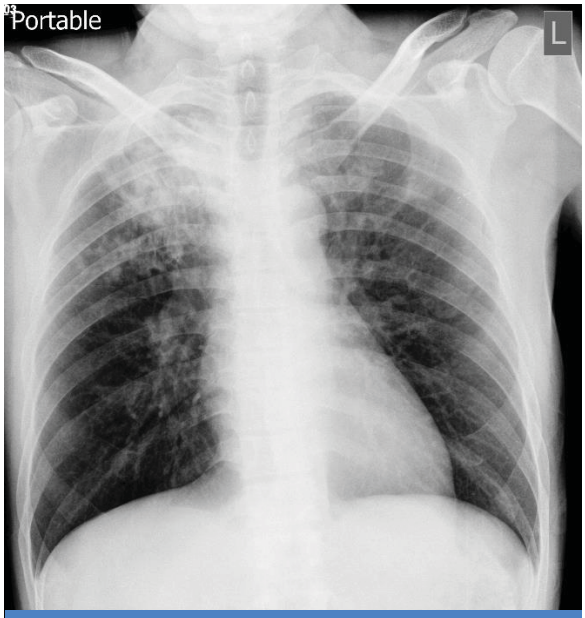
Lancet 2011; 377: 147–52
Published Online
December 9, 2010
DOI:10.1016/S0140-6736(10)61972-1
See Comment page 103

- 359 contacts with active tuberculosis
- 142 (40%) had had isolates tested for resistance against first-line drugs
- 129 (90·9%) had MDR tuberculosis

2. 曾為RMP抗藥及MDR-TB接觸者之個案-2

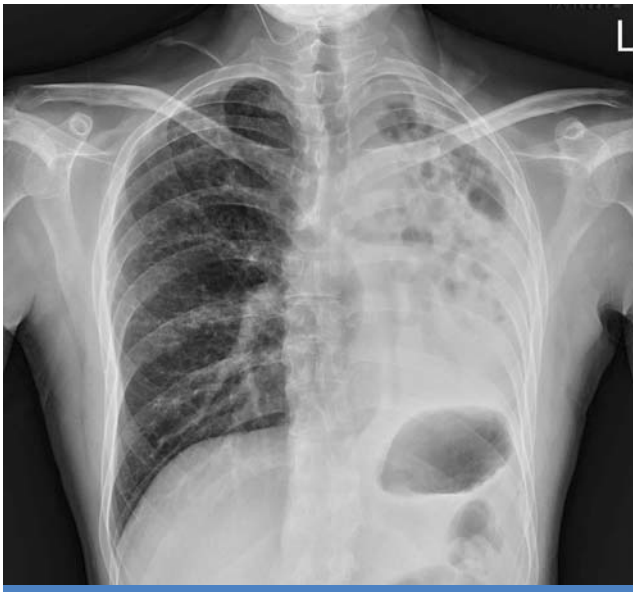


Family Hx of MDR-TB (+)
MDR-TB: 46 days

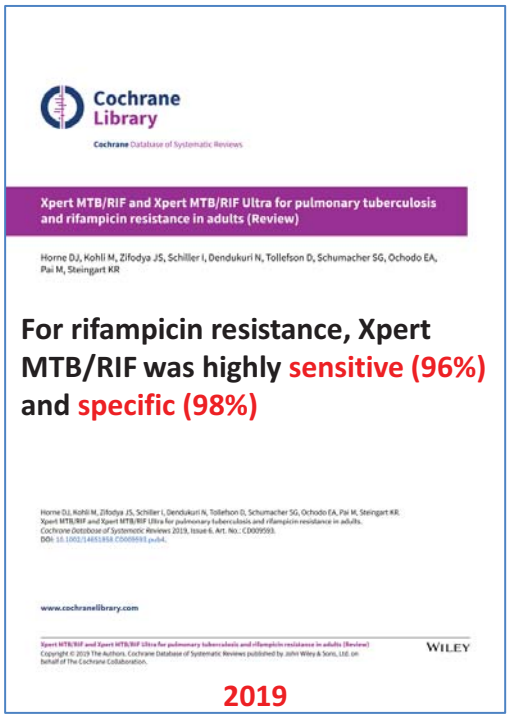


Family Hx of MDR-TB (+)
Genotypic DST: HR-R

3. 臨床經分子快速檢測為RMP抗藥之結核病個案



No known risk
X-pert: RMP-resistant (+)
Phenotypic DST: RMP-resistant


Cochrane Library
Cochrane Database of Systematic Reviews

Xpert MTB/RIF and Xpert MTB/RIF Ultra for pulmonary tuberculosis and rifampicin resistance in adults (Review)

Horne DJ, Kohli M, Zifodya JS, Schiller I, Dendukuri N, Tollefson D, Schumacher SG, Ochodo EA, Pai M, Steingart KR

For rifampicin resistance, Xpert MTB/RIF was highly sensitive (96%) and specific (98%)

www.cochranelibrary.com

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2019

Diagnosis of Tuberculosis in Adults and Children

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines

- The sensitivity and specificity of rapid molecular DST for detecting **rifampin resistance** are both >97%, indicating that false-positive and false-negative results occur <3% of the time
- The sensitivity and specificity of rapid molecular DST for detecting **isoniazid resistance** are estimated to be 90% and 99%, respectively, indicating that false-positive and false-negative results occur roughly 1% and 10% of the time, respectively
- Confirmation of a positive test result for rifampin resistance has been recommended
  - To confirm a positive result, genetic loci associated with rifampin resistance (to include *rpoB*), as well as isoniazid resistance (to include *inhA* and *katG*), should be sequenced to assess for MDR-TB

Clin Infect Dis 2017;64:e1–e33

抗藥性的判定建議-1

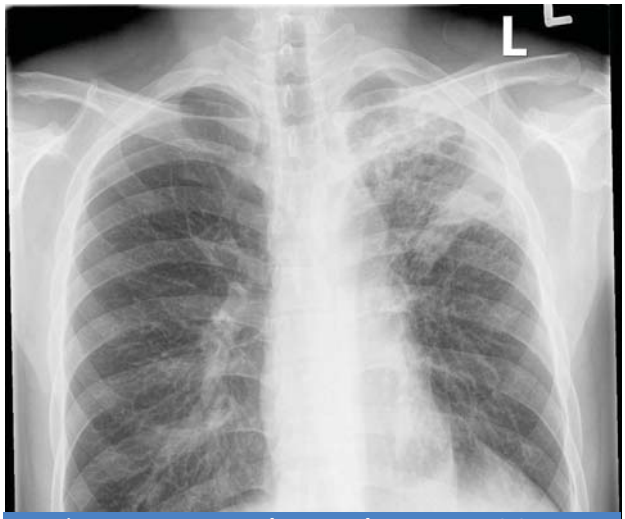
- **分子檢驗呈Rifampicin敏感**
  - Rifampicin可能有效，並等待傳統藥物的感受性試驗結果
- **分子檢驗呈Rifampicin抗藥**
  - **多重抗藥性或Rifampicin抗藥性高危險群**
    - 先診斷 為Rifampicin抗藥
    - 使用其他分子方法，來確認抗藥性基因位點(isoniazid及rifampicin)
    - 進行Pyrazinamide、針劑注射藥物(Amikacin, Kanamycin及 Capreomycin)及Fluoroquinolone類藥物的分子檢測
  - **多重抗藥性或Rifampicin抗藥性低危險群**
    - 使用分子測驗再次確認是否為rifampin抗藥
    - 若第二次檢驗Rifampicin仍為抗藥性，可先診斷為抗藥
    - 若第二次檢驗結果Rifampicin為敏感，先視為rifampicin敏感
    - 將菌株送至疾病管制署參考實驗室進行傳統藥物感受性試驗(包含：液態最低抑菌濃度測試法及固態比例法)再確認

台灣結核病診治指引第7版，2021

抗藥性的判定建議-2

- 分子檢驗為rifampicin抗藥，但傳統藥物感受性試驗呈現敏感
  - 臺灣rifampcin抗藥及多重抗藥結核病個案的結核分枝桿菌，約有9 %的菌株於*rpoB*基因發生爭議性突變，或為silent 突變，或是傳統液態藥敏有rifampicin偽陰性
  - 傳統藥物感受性試驗(包含：液態最低抑菌濃度測試法及固態比例法)再確認

台灣結核病診治指引第7版，2021



- 1st TB history: 2016/7~2017/1 with HRZ(E) Phenotypic DST: all susceptible
- 2nd TB history: 2017/9, relapse
- Genotypic DST: RMP-R
- Phenotypic DST: all susceptible
- Genetic locus: *rpoB* L511P

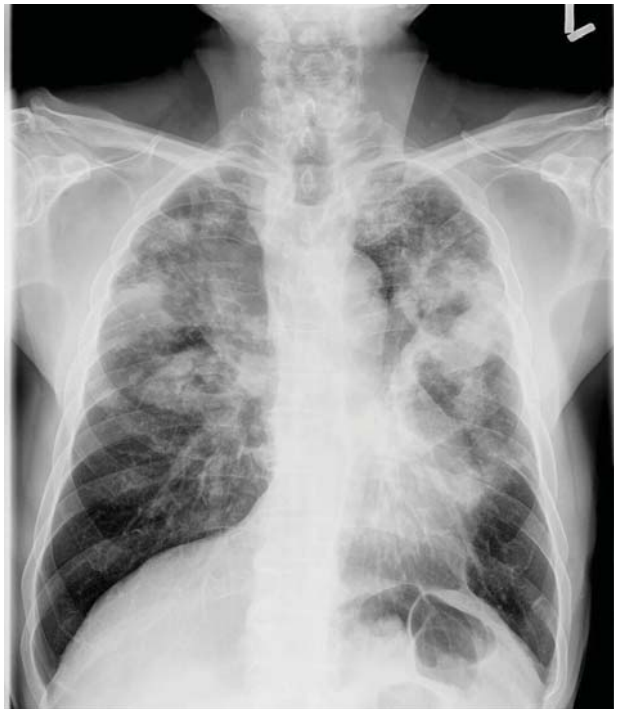
4. 抗藥性高風險地區新發個案-1

110年度抗藥性結核病高風險地區(依據10804-10909疫情分析)

管理單位	TB新案	RR/MDR-TB新案	RR/MDR-TB新案占百分比	110年變更情形
臺中市外埔區	24	0	0.0%	移出高風險鄉鎮
雲林縣東勢鄉	22	0	0.0%	
苗栗縣苗栗市	44	0	0.0%	維持為高風險地區 (列入觀察名單)
嘉義縣民雄鄉	32	1	3.1%	
基隆市七堵區	45	1	2.2%	
花蓮縣吉安鄉	52	1	1.9%	
臺中市西　區	62	1	1.6%	
新北市深坑區	7	1	14.3%	維持為高風險地區
花蓮縣萬榮鄉	12	1	8.3%	
基隆市仁愛區	21	1	4.8%	
嘉義縣太保市	21	1	4.8%	
屏東縣恆春鎮	25	1	4.0%	
臺東縣鹿野鄉	10	2	20.0%	新增為高風險鄉鎮區
彰化縣秀水鄉	26	3	11.5%	
南投縣信義鄉	31	3	9.7%	
南投縣竹山鎮	26	2	7.7%	
苗栗縣頭份市	33	2	6.1%	
臺南市新營區	46	2	4.3%	
桃園市蘆竹區	46	2	4.3%	
新北市泰山區	46	2	4.3%	
屏東縣潮州鎮	48	2	4.2%	
全國資料	12,602	151	1.20%	

備註：已排除外國人及同住接觸者發病

4. 抗藥性高風險地區新發個案-2

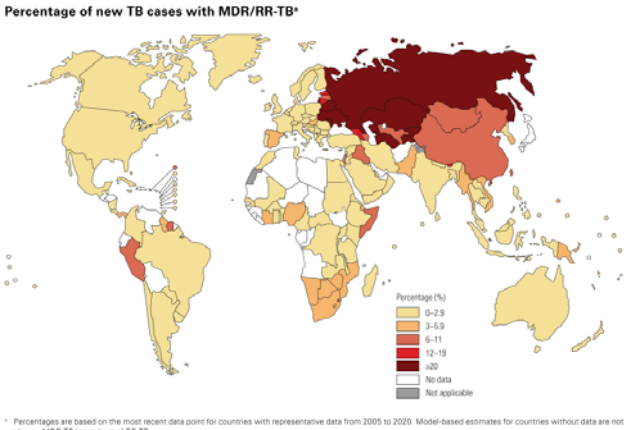


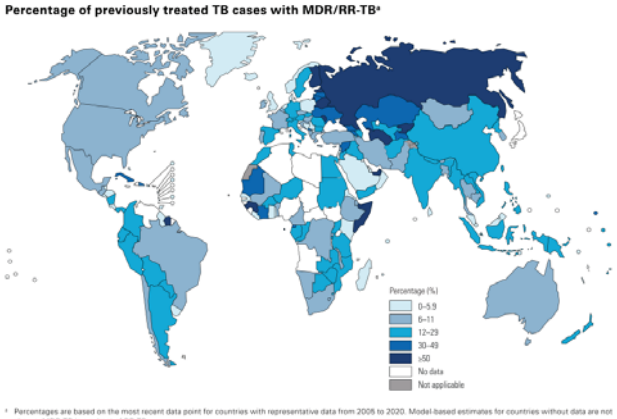
- 70 y/o, male
- No previous TB Hx
- No RR/MDR-TB contact
- Sputum AFS(++++)
- Xpert: MTB(+), RMP-R (+)
- Phenotypic DST: Rifampicin-resistant (35 days)

5. 民國80年後，具WHO公布之TB或MDR-TB 高負擔國家居住經驗者(一年內累計達一個月以上)-1

Globally, 2019

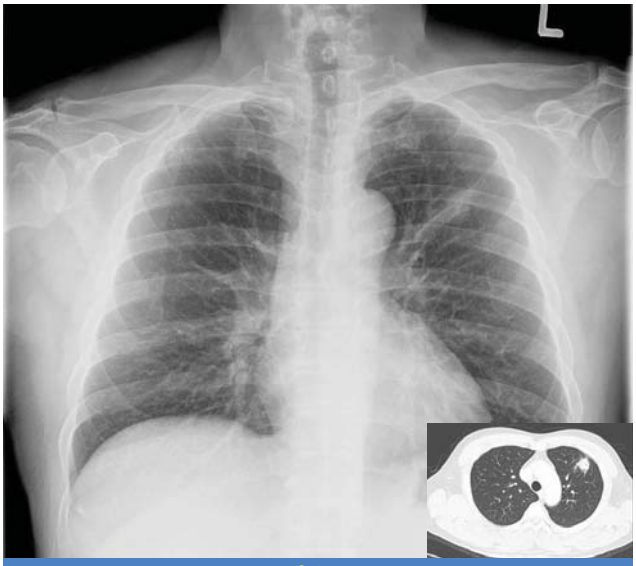
3.3% of new TB cases and 17.7% of previously treated cases had MDR/RR-TB



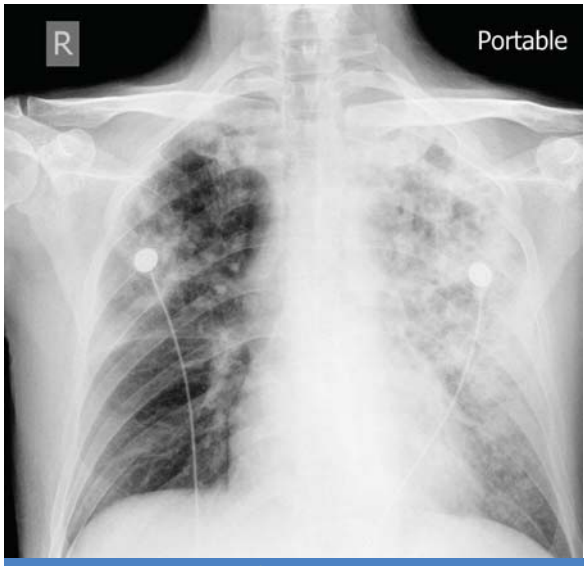


Global tuberculosis report 2020

5. 民國80年後，具WHO公布之TB或MDR-TB高負擔國家居住經驗者(一年內累計達一個月以上)-2



China
Sputum AFS(+); Xpert: RMP-R
GenoTypeMTBDR*plus* test: HR-R
Phenotypic DST: HR-R (44 days later)



Vietnam
Sputum AFS(++++); Xpert: RMP-R
GenoTypeMTBDR*plus* test: HR-R
Phenotypic DST: HERS-R (40 days later)

6. 治療2個月之痰培養仍為陽性者-1

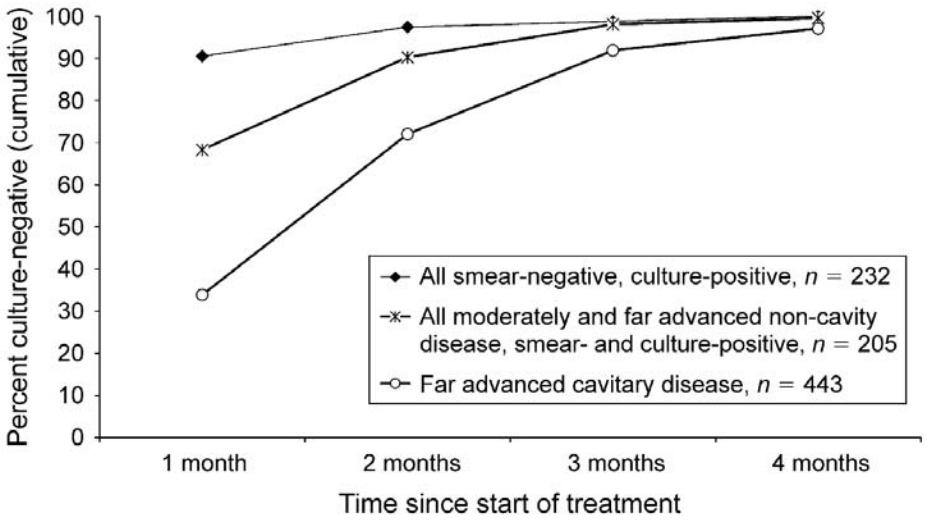


Figure 5.2 Culture conversion in initially culture-positive pulmonary tuberculosis, by type and severity of disease. (Data from Damien Foundation Bangladesh cohort, 1994–2007.)

Guidelines for Clinical and Operational Management of Drug-Resistant Tuberculosis, IUATLD, 2013

6. 治療2個月之痰培養仍為陽性者-2

- The culture result of a sputum specimen obtained at the completion of the intensive phase of treatment (2 months)
  - Correlate with the likelihood of relapse
    - Albeit with low sensitivity

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB, 2016

Sputum monitoring during tuberculosis treatment for predicting outcome: systematic review and meta-analysis

David J Horne, Sarah E Royce, Lisa Gooze, Masahiro Narita, Philip C Hopewell, Payam Nahid, Karen R Steingart

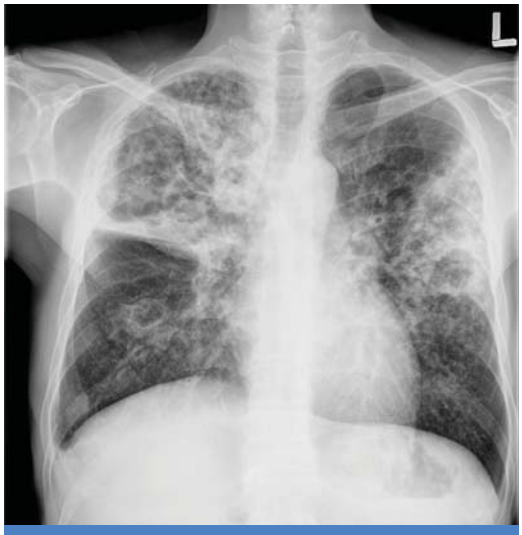
WHO has previously recommended sputum-smear examination at the end of the second month of treatment in patients with recently diagnosed pulmonary tuberculosis, and, if positive, extension of the intensive therapy phase. We did a systematic review and meta-analysis to assess the accuracy of a positive sputum smear or culture during treatment for predicting failure or relapse in pulmonary tuberculosis. We searched PubMed, Embase, and the Cochrane Library for studies published in English through December, 2009. We included randomised controlled trials, cohort, and case-control studies of previously untreated pulmonary tuberculosis patients who had received a standardised regimen with rifampicin in the initial phase. Accuracy results were summarised in forest plots and pooled by use of a hierarchical regression approach. 15 papers (28 studies) met the inclusion criteria. The pooled sensitivities for both 2-month smear (24% [95% CI 12–42%], six studies) and culture (40% [95% CI 25–56%], four studies) to predict relapse were low. Corresponding specificities (85% [95% CI 72–90%] and 85% [95% CI 77–91%]) were higher, but modest. For failure, 2-month smear (seven studies) had low sensitivity (57% [95% CI 41–73%]) and higher, although modest, specificity (81% [95% CI 72–87%]). Both sputum-smear microscopy and mycobacterial culture during tuberculosis treatment have low sensitivity and modest specificity for predicting failure and relapse. Although we pooled a diverse group of patients, the individual studies had similar performance characteristics. Better predictive markers are needed.

- Both sputum-smear microscopy and mycobacterial culture during tuberculosis treatment have low sensitivity and modest specificity for predicting failure and relapse

Lancet Infect Dis 2010;10:387–94

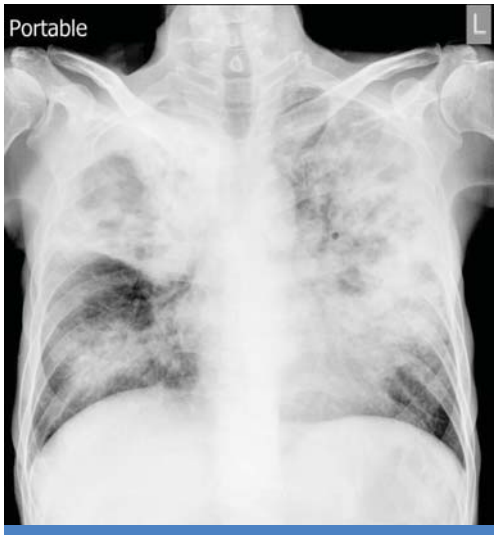
6. 治療2個月之痰培養仍為陽性者-3

開始治療



Acid-fast stain (4+), Xpert: no RMP-R
DST: all susceptible (33 days)

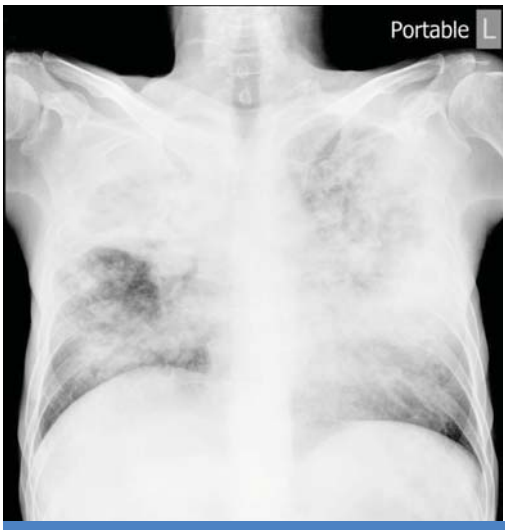
治療1個月



Acid-fast stain (4+)

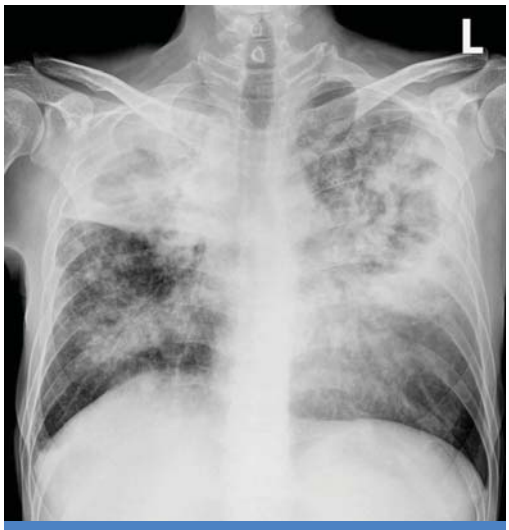
6. 治療2個月之痰培養仍為陽性者-4

治療2個月



Sputum AFS (4+)
Xpert: MTB(+), no RMP-R

治療3個月



Sputum AFS (4+)
DST: all susceptible (59 days)

台灣結核病診治指引

舊版

- 第1次培養陽性的結核菌株
- 治療第5個月仍呈陽性
- 陰轉後再度培養陽性

2021

- 第1次培養陽性的結核菌株
- 治療滿2個月仍呈陽性
- 陰轉後再度培養陽性

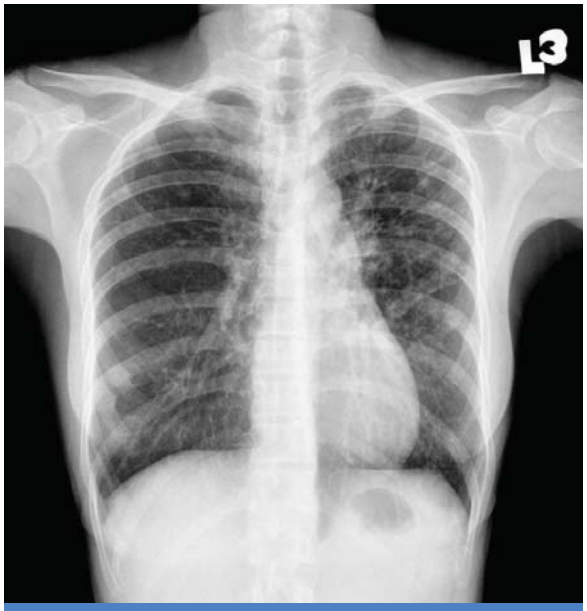
7. INH抗藥，擬申請二線藥者-1

- 1. RIF，EMB，PZA，±INH 6個月
- 2. RIF，EMB，PZA，±INH，加上一種近代的 (FQ)(如 moxifloxacin, levofloxacin)，amikacin/kanamycin
- 3. 個人化治療方案
  - 無法耐受INH、RIF、EMB、PZA中的某些藥物時，採以病人可以耐受的4種藥組成個人化治療方案

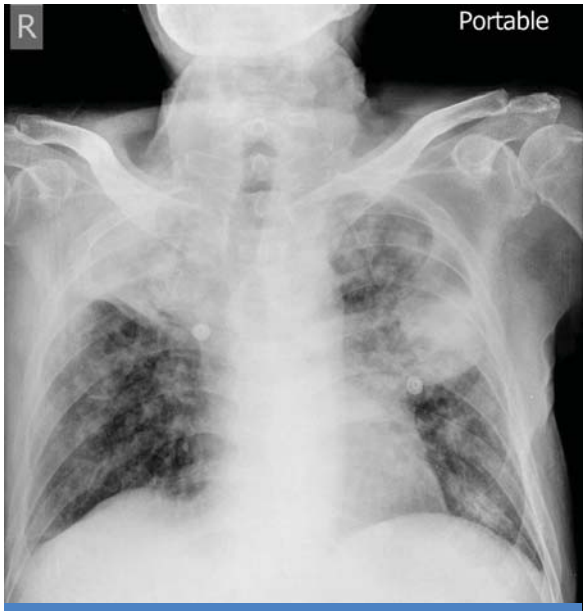
- INH抗藥/修改處方
  - DST結果是否正確/可靠？
  - 從取痰到取得DST結果期間，有沒有可能因為治療而產生rifampicin抗藥？
  - 如何降低INH抗藥病人失敗或復發的風險？
- 如果治療反應不佳考慮加藥，建議以GeneXpert檢驗是否已有rifampicin抗藥

台灣結核病診治指引第7版，2021

7. INH抗藥，擬申請二線藥者-2

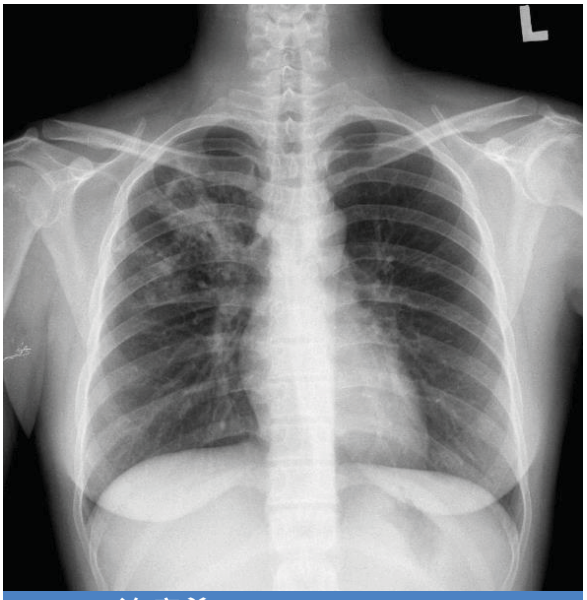


HERZ
DST:HS-R (42 days later)

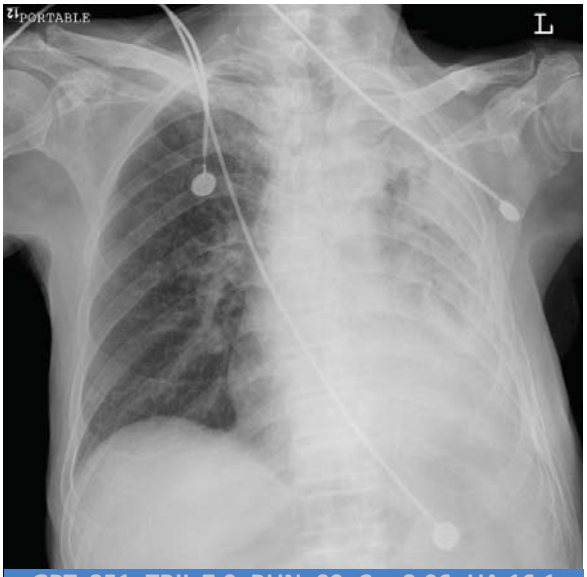


2HERZ (DST:HS-R)
AFS (4+), Xpert : MTB (+) , no RMP-R

8. 因藥物副作用，擬申請二線藥者



治療前Uric acid 7.4 mg/dL
治療1星期Gouty attack: 15.7 mg/dL
DC PZA, Keep HER



GPT: 251, TBIL:7.0, BUN: 99, Cre:3.06, UA:16.1
RMP: Hepatitis; PZA: Hyperuricemia
HE + Rifabutin + Levofloxacin + SM
RMP-resistant

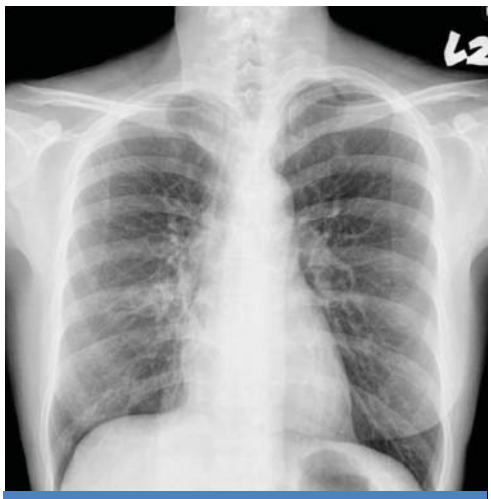
9. 通報結核病之畜牧場人員

- 畜牧場或屠宰場發現牛結核動物，農委會防檢局將通知疾管署，並轉由衛生局提供該畜牧場或屠宰場接觸人員相關衛教，建議其接受胸部X光檢查，並進行後續監測
- 有接觸史人員通報結核病時，衛生局即能掌握個案，並即時送驗痰液，進行分子快速抗藥性測試
  - 及早診斷，給予適當治療處方
  - 進行菌株鑑定，確認是否為感染牛結核菌

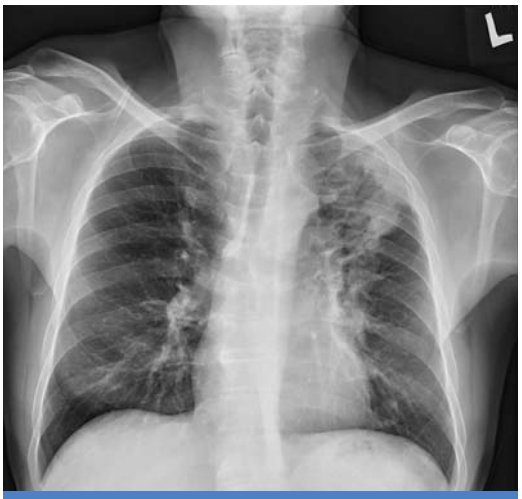
10. *M. bovis*結核個案或動物之接觸者轉為個案者-1

- 牛結核病的治療與一般結核病相似
  - 但牛結核菌對於抗結核菌藥物Pyrazinamide (PZA)有抗藥性
  - 治療期程需延長至9個月
  - 相關動物接觸史
  - 及早送驗分子快篩

10. *M. bovis*結核個案或動物之接觸者轉為個案者-2



PZA: resistant
Low-level INH-resistant



PZA+ INH: resistant
DST: ERS + FQs + KM-susceptible

11. 潛伏結核感染治療個案結核病發病者-1

Isoniazid Preventive Therapy and Risk for Resistant Tuberculosis

Maria Elvira Balcells,*† Sara L. Thomas,* Peter Godfrey-Faussett,* and Alison D. Grant*

In the context of tuberculosis (TB) resurgence, isoniazid preventive therapy (IPT) is increasingly promoted, but concerns about the risk for development of isoniazid-resistant tuberculosis may hinder its widespread implementation. We conducted a systematic review of data published since 1951 to assess the effect of primary IPT on the risk for isoniazid-resistant TB. Different definitions of isoniazid resistance were used, which affected summary effect estimates; we report the most consistent results. When all 13 studies (N = 18,095 persons in isoniazid groups and N = 17,985 persons in control groups) were combined, the summary relative risk for resistance was 1.45 (95% confidence interval 0.85–2.47). Results were similar when studies of HIV-uninfected and HIV-infected persons were considered separately. Analyses were limited by small numbers and incomplete testing of isolates, but findings do not exclude an increased risk for isoniazid-resistant TB after IPT. The diagnosis of active TB should be excluded before IPT. Continued surveillance for isoniazid resistance is essential.

Emerg Infect Dis 2006;12:744-751

- Summary relative risks for isoniazid-resistant TB after IPT
  - Not statistically significant
- Limited by small numbers and incomplete testing of isolates
  - Positive cultures tested for resistance varied from 37% to 100%
- Do not exclude an increased risk for isoniazid-resistant TB after IPT
- The main reason for the development of resistance
  - Failure to diagnose active TB ?

11. 潛伏結核感染治療個案結核病發病者-2

Rifampicin resistance after treatment for latent tuberculous infection: a systematic review and meta-analysis

S. den Boon,* A. Matteelli,† H. Getahun†

*Independent consultant, Geneva, †The Global TB Programme, World Health Organization, Geneva, Switzerland

SUMMARY

SETTING: Treatment for latent tuberculous infection (LTBI) reduces the risk of tuberculosis (TB) disease. Shorter, rifamycin-containing regimens have been shown to be as effective as 6 months of isoniazid and superior with regard to safety and completion rate. It is unknown whether preventive therapy with rifamycins increases resistance to the drugs used.

OBJECTIVE: To determine whether treatment for LTBI with rifamycin-containing regimens leads to significant development of resistance against rifamycins.

DESIGN: Systematic review and meta-analysis.

RESULTS: We included six randomised-controlled trials of rifamycin-containing regimens for LTBI treatment that reported drug resistance. There was no statistically significant increased risk of rifamycin resistance after LTBI treatment with rifamycin-containing regimens compared to non-rifamycin-containing regimens (RR 3.45, 95%CI 0.72–16.56; $P = 0.12$) or placebo (RR 0.20, 95%CI 0.02–1.66; $P = 0.13$).

CONCLUSION: Preventive treatment with rifamycin-containing regimens does not significantly increase rifamycin resistance. Programmatic management of LTBI requires the creation of sound surveillance systems to monitor drug resistance.

KEY WORDS: chemoprophylaxis; prevention; rifamycin

Int J Tuberc Lung Dis 2016;20:1065–1071

- Preventive treatment with rifamycin-containing regimens does not significantly increase rifamycin resistance
  - The number of resistant cases that were found was very small
- Programmatic management of LTBI requires the creation of sound surveillance systems to monitor drug resistance

11. 潛伏結核感染治療個案結核病發病者-3

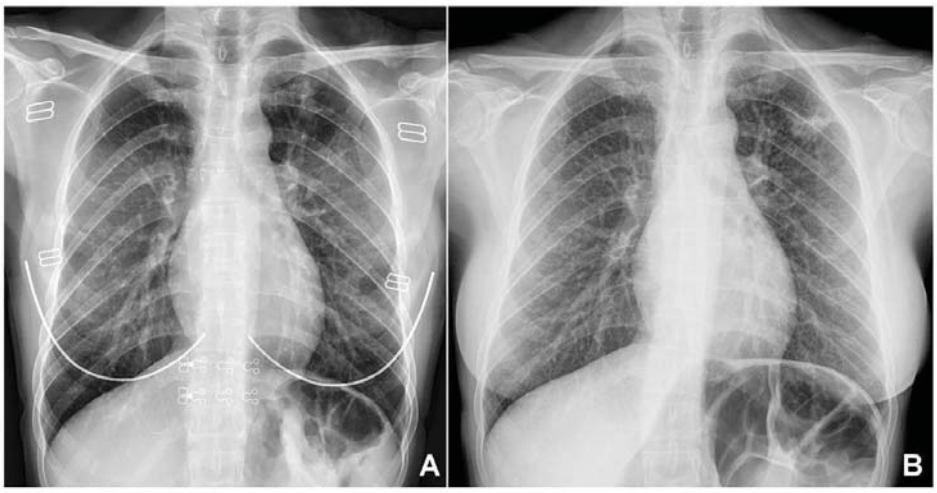


Figure 2 Chest radiography images (**A**) before and (**B**) after nine months of isoniazid treatment for the patient who progressed to active disease following the latent tuberculosis infection treatment.

Infect Drug Resist 2021;14:1505-9

分子檢測的其他考量

處方的調整與分子抗藥檢測

- **處方調整原則**
  - 同時多種有效的藥物
  - 藥物的強度
  - 病灶嚴重度
- **調整的時機**
  - 開始治療
  - 治療中
- **需要藥敏嗎？**
  - 急著要嗎？
- **可檢驗藥物**
  - Isoniazid/Rifampicin
  - Fluoroquinolone (moxifloxacin/levofloxacin)
  - 2nd line injectable drugs
  - Pyrazinamide
- **執行分子檢測的檢驗室**
  - 自己做
  - 外送：代檢/CDC
- **經費來源**
  - 健保
  - 自費

結核病檢驗

結核病代檢合約實驗室

- 2020年10家合約實驗室檢測占整體比例
  - 痰塗片41.2%
  - 培養40.0%
  - 鑑定45.1%
  - 藥物感受性試驗39.8%

- 由國內外實驗室認證機構（如TAF、CAP等）認證參加疾管署、醫檢學會等單位之能力試驗外部品管，疾管署支付實驗室部分維持費及補貼檢驗費。

結核病認可傳染病檢驗機構

- 衛生福利部核發為期4年的認可證書，授權機構執行結核病確定檢驗
- 截至2021年2月17日止，共39家認可實驗室；接受定期能力試驗及不定期現場查核。

認可實驗室

結核病檢驗認可實驗室　109年10月30日更新

序號	機構名稱	縣市別	結核病檢驗認可	結核病檢驗認可方法
1	衛生福利部胸腔病院	臺南市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測
2	衛生福利部桃園醫院	桃園市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/細胞激素檢測
3	臺中榮民總醫院	臺中市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/細胞激素檢測
4	高雄榮民總醫院	高雄市	■	病原體分離、鑑定/鏡檢+病原體分生檢測/Xpert 分生檢測
5	長庚醫療財團法人高雄長庚紀念醫院	高雄市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
6	國立成功大學醫學院附設醫院	臺南市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
7	天主教耕莘醫療財團法人天主教耕莘醫院	新北市	■	病原體分離、鑑定/鏡檢+病原體分生檢測/Xpert 分生檢測
8	新光醫療財團法人新光吳火獅紀念醫院	臺北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
9	戴德森醫療財團法人嘉義基督教醫院	嘉義市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
10	中國醫藥大學附設醫院	臺中市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測
11	佛教慈濟醫療財團法人花蓮慈濟醫院	花蓮縣	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測
12	臺北市立萬芳醫院-委託財團法人臺北醫學大學辦理	臺北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測
13	臺北市立聯合醫院林森中醫昆明(昆明)院區	臺北市	■	病原體分離、鑑定/鏡檢+病原體分生檢測/藥物感受性試驗
14	財團法人私立高雄醫學大學附設中和紀念醫院	高雄市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
15	中山醫學大學附設醫院	臺中市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測
16	台美醫事檢驗所	新北市	■	病原體分離、鑑定/藥物感受性試驗
17	國立臺灣大學醫學院附設醫院新竹分院	新竹市	■	Xpert分生檢測
18	安泰醫療社團法人安泰醫院	屏東縣	■	Xpert分生檢測
19	財團法人天主教靈醫會羅東聖母醫院	宜蘭縣	■	Xpert分生檢測
20	台灣基督長老教會馬偕醫療財團法人淡水馬偕紀念醫院	新北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
21	彰化基督教醫療財團法人彰化基督教醫院	彰化縣	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/細胞激素檢測
22	衛生福利部彰化醫院	彰化縣	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/細胞激素檢測/Xpert 分生檢測
23	英秀士醫事檢驗所	臺中市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
24	國立臺灣大學醫學院附設醫院	臺北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
25	佛教慈濟醫療財團法人大林慈濟醫院	嘉義縣	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測

- 若高風險對象於認可實驗室完成GeneXpert檢驗
  - 可不必重覆送至三總檢驗
  - 如檢驗結果為RMP抗藥
    - 再行送至三總進行其他一線（如INH）及二線藥物之分子快速藥敏檢測

結核病檢驗認可實驗室　109年10月30日更新

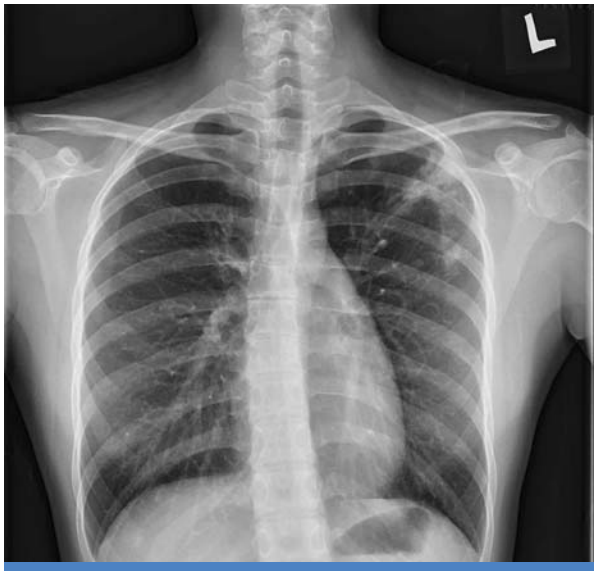
26	義大醫療財團法人義大醫院	高雄市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert分生檢測
27	醫療財團法人徐元智先生醫藥基金會亞東紀念醫院	新北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
28	長庚醫療財團法人嘉義長庚紀念醫院	嘉義縣	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
29	三軍總醫院附設民眾診療服務處	臺北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
30	奇美醫療財團法人奇美醫院	臺南市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測/Xpert 分生檢測
31	長庚醫療財團法人基隆長庚紀念醫院	基隆市	■	病原體分離、鑑定/藥物感受性試驗
32	長庚醫療財團法人林口長庚紀念醫院	桃園市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
33	屏基醫療財團法人屏東基督教醫院	屏東縣	■	Xpert分生檢測
34	國泰醫療財團法人沙止國泰綜合醫院	新北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
35	臺北榮民總醫院	臺北市	■	病原體分離、鑑定/藥物感受性試驗/鏡檢+病原體分生檢測
36	衛生福利部臺東醫院	臺東縣	■	鏡檢+病原體分生檢測
37	佛教慈濟醫療財團法人台北慈濟醫院	新北市	■	病原體分離、鑑定/鏡檢+病原體分生檢測

疾病管制署指定實驗室

對象	檢測方式
1. 結核病再治個案（失落、失敗、復發，重開非復發曾經使用抗結核藥物4週以上）	1.以GeneXpert，就RMP進行檢測 2.如為RMP抗藥: (1)以GenoType MTBDR*plus*，就RMP及INH進行檢測，及 (2)GenoType MTBDR*sl*，就FLQ及二線藥針劑進行檢測
2. RMP抗藥及多重抗藥性結核病個案之接觸者轉為個案者[註]	
3. 經分子快速檢測為RMP抗藥之結核病個案	
4. 本署指定之抗藥性結核病高風險地區之新發生個案	
5. 個案於80年後，曾經停留在世界衛生組織公布之結核病或多重抗藥性結核病高負擔國家，且停留天數於一年內累積達1個月（30天）以上者（非限於通報前一年）	
6. 治療2個月之痰培養仍為陽性者	
7. INH抗藥，擬申請二線藥者	
8. 因藥物副作用，擬申請二線藥者	
9. 通報結核病之畜牧場人員	1.以GenoType MTBDR*plus*，就RMP及INH進行檢測 2.如任一抗藥者，再以GenoType MTBDR*sl*，就FLQ及二線藥針劑進行檢測
10 M. bovis結核個案或動物之接觸者轉為個案者	
11 潛伏結核感染治療（LTBI）個案結核病發病者[註]	

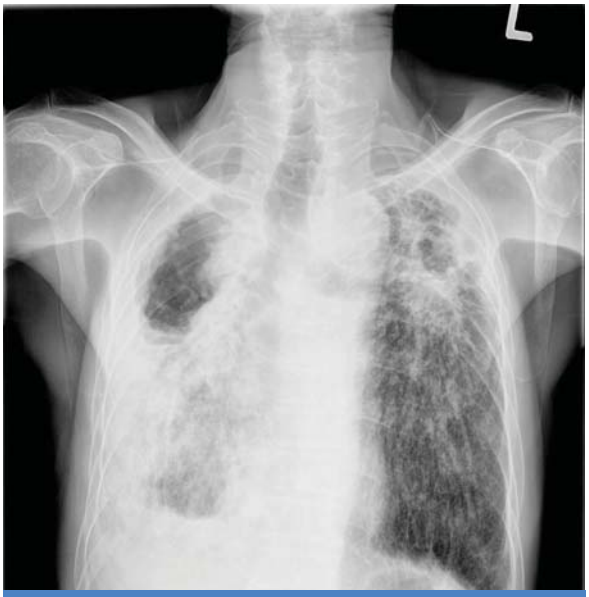
註：若個案同時符合對象2及對象11之分子快速檢測條件，請優先以對象2之檢測方式優先進行GeneXpert檢測，如有RMP抗藥再進行GenoType。

某校園TB事件



Sputum AFS (-)
X-pert: MTB(+), no RMP-R
Phenotypic DST: HERS-S (45 days later)

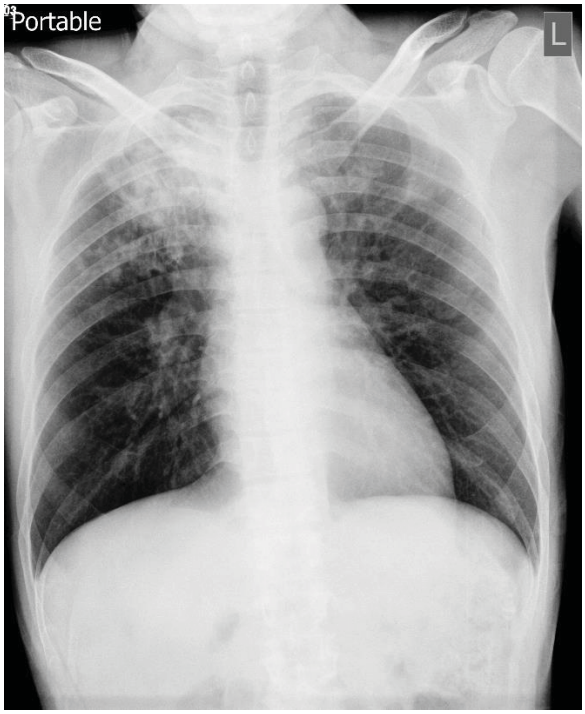
健保？自費？外送？



Pneumoconiosis, Sputum AFS(++++)
Xpert: MTB(+), RMP-resistant (-)
Phenotypic DST: all susceptible (1 month)

結論

精準醫療：分子抗藥檢測已經來臨-1



- Family Hx of MDR-TB (+)
- X-pert: MTB, RMP-resistant
- The designated laboratory
  - Genotypic DST
    - HR: R; FQ/SLID: susceptible
- CDC laboratory
  - PZA: susceptible
  - Genetic mutation loci
    - *rpoB* S531L and *inhA* C-15T
- Phenotypic DST
  - High-level H-S, Low-level H-R, RS-R, E-S
  - Second-line drugs: all susceptible, except ethionamide-R, Rifabutin-R

精準醫療：分子抗藥檢測已經來臨-2

- **特定高危險族群**
  - 技術進步，逐步擴展
- **Rifampicin抗藥**
  - 確認isoniazid是否抗藥
  - 確認isoniazid及rifampicin的抗藥性基因位點
  - 進行注射藥物(amikacin, kanamycin及 capreomycin)、Fluoroquinolone類藥物及Pyrazinamide的分子檢測
- **善用TB代檢網**
  - 疾病管制署指定實驗室/合約實驗室

分子快速檢測送驗對象-2021

- 結核病再治個案
- 曾為RMP抗藥及MDR-TB接觸者之個案
- 臨床經分子快速檢測為RMP抗藥之結核病個案
- 抗藥性高風險地區新發個案
- 具WHO公布之TB或MDR-TB高負擔國家居住經驗者
- 治療2個月之痰培養仍為陽性者
- INH抗藥，擬申請二線藥者
- 因藥物副作用，擬申請二線藥者
- 通報結核病之畜牧場人員
- *M. bovis*結核個案或動物之接觸者轉為個案者
- 潛伏結核感染治療個案結核病發病者

感謝聆聽 敬請指導